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Human mutant prese
Human mutant prese
AD4/AD31P sequence
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Tumour suppressor
Presentlin homolog
Drosophila melanog
                             Presentlin coding
Presentlin-1-1 wil
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Human AD4 protein
Full AD4/AD3LP seq
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Human presentlin I
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         9
                                                                                                                                                                                                                                                                                                                                                                                                             The sel-12 gene (AAT60306) of Caenorhabditis elegans (CE) encodes a polypeptide (AAM14006) that displays about 50% amino acid sequence identity to human presentlin PS1 and PS2 proteins associated with Alzheimer's disease (AD). Like presentlins, sel-12 is widely expressed in neural and non-neural cells. The gene was identified by screening for suppressors of the 'Multivulva' phenotype of CE caused by an allele of lin-12 that causes constitutive Lin-12 activation. 2 Recessive suppressors, ari31 and ari33, proved to be alleles of the new gene (sel means suppressor and/or enhancer of lin-12). The gene can be used to produce wild-type or mutated (see also AAM14007) SEL-12 in host cells, in methods for screening for extragenic suppressors or enhancers of a SEL-12 allele, and in the development of transgenic animals, esp. transgenic CE, useful in
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          GTTTAATTACCCAAGTTTGAGATGCCTTCCACAAGGAGACAACAGGAGGCGGAGGTGCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        GATGCGGAAACACATACCGTTTACGGTACAAATCTGATAACAAATCGGAATAGCCAAGAA
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                                                                                                                                                                                                                                                                                                                                                New isolated SEL-12 presentlin gene - used to develop products for the diagnosis and prophylactic or therapeutic treatment of disorders such as Alzheimer's disease
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                                                                                        ullin; transgenic animal; Alzheimer's disease; therapy; diagnosis; ss.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Sequence 1500 BP; 403 A; 312 C; 314 G; 471 T; 0 other;
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100.0%; Pred. No. 0;
ive 0; Mismatches
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                                                                                                                                          Location/Qualifiers
22..1407
/*tag= a
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                                                              Caenorhabditis elegans SEL-12 gene
    ВР
                                                                                                                                                                                                                                                                         (UYCO ) UNIV COLUMBIA NEW YORK
  AAT60306 standard; DNA; 1500
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                                              entry)
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Matches 1500; Conservative
                                                                                                                    Caenorhabditis elegans.
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P-PSDB; AAW14006.
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Page 3

Db 1699 CTATARATACAAGTTTTATAAGCTTATTCATGGATGGCTTATTGTTCTTCT	4 (	DD 1/39 ICITITCCIAITCACIACAAICTAGGGAGTAAGITGATATTACTATTCTCATAAA	-	Qy 522 TTTGTTTGGACTGGGAAGGACTCTCGGAATGATGTGTATACATTGGAAAGGTCC	Db 1879 TTTGTTTGGACTGGGTAACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAGGTC	Qy 582 ATTGCGTCTGCAACAGTTCTACCTTATTACAATGTCTGCACTAATGGCTCTGGTCTTTAT 	642	199	Oy 702 GGTTGCCGTGCTCACAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAG 1111111111111111111111111111	Qy 762 AAACGAGCCAATTTCCCGGCGCTGATTTATTCGT	Db 2119 AAACGAGCCATTTTCCCGGCGCTGATTATCGTGTAAGTTTCCTAATTTATGGAATTA	Qy 797CTGGAGTCATCTATCCTAGGTT	Db 2179 ATATICAIGACGITICAAATICIAAAACAITITCAGCIGGAGICAICTAICCCIACGITC	82	2239	DD 2299 GTGAGTATCACCTAAAATTTTCGAATTTTTATTATCCAAAATTTTCGAAATTTTTATATTCCAAAATTTTCAAACTTTCAAAACTTTTCGAAATTTTTCAAAACTTTTCGAAATTTTTATATTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTCAAAATTTTAAAATTTTCAAAATTTTAAAATTTTAAAATTTTAAAATTTTAAAATTTT	Qy         892         TTTCCTGGAGAGGCGAGTTGTTCATCTGAAACGCCAAAACGGCCAAAAGTGAAACGAATT           IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	Qy 952 CCTCAAAAAGTGCAAATCGAATACTACAACTTCAACGACACAAAACTCTGGAGTA	Db   2419   CCTCAAAAGTGGAATGCGAATACTACAGGTTCAACGACACAAAACTCTGGGGCTA     Qy	Qy 1072 CACGAAGAGGAGAGGGTGTGAAA 1098	Db 2539 CACGAAGAGAGAGAGTGAGTGAAAA 2565	RESULT 3 AAT59536 ID AAT59536 standard; cDNA; 1750 BP	S	Human early onset Alzheimer's disease (EOAD) splice variant gen	Kw Early Onset Alzheimer's disease: EOAD: neurodegenerative disease.
Qy 1321 TTACACAAGTCTCTCAAAAGTGTTTATTATTAATTCTCTGTTTTGCCATTTCTTTGC 1380	Db 1321 TTACACAAGTCTCTCAAAAGTGTTTATTATTATTATTATTATTTGCCTGTTTTTGCCATTTCTTTGC 1380 Oy 1381 ATCATCAACAACTTTTGCATTATATTATTATTATTAAAAATTCTCTGTTTTTGCCATTTCTTTGC 1340	1381 ATCATCAACTTTTCGATTATATATATCTTGACCAATCTCAAACCTTTATATTTACATATTTACTTATATTTTACTTACATTTTACTTACTTATATTTTACTTACTTATATTTTACTTACTTACTTATATTTTACTTACTATTTTACTTACTATTTTACTTACTATTTTACTTACTAC	ATTTTGAACTTTGTCATTTAAGTTATAAATAAATTTAAAAAAAA	Db 1441 ATTTTGAACTTTGTCATTTAAGTTATAAATAATTAAAAAAAA	RESULT 2	AAL47322 ID AAL47322 standard; DNA; 4137 BP. XX	AAL47322;	DT 02-SEP-2002 (first entry) XX DE C elegans sel-12 gene promoter and requisions remines	Se	os Caenorhabditis elegans.	n use376239-B1. XX	PD 23-APR-2002.	PF 04-APR-1997; 97US-0832867. XX	PR 04-APR-1997; 97US-0832867	PI Baumeister R:	WPI; 2002-4	I Isolated DNA molecule comprising promoter of the sel-12 gene from Caenorhabditis elegans operably linked to heterologous gene, directs expression in neural cells and is useful to develop drugs to treat neuronal disorders -	Claim 1; Fig 3; 78pp; English.	The present invention relates to DNA molecules comprising the promoter of the sel-12 gene from Caenorhabditis elegans operably linked to a CC the reterologous DNA sequence encoding a protein of interest. The sequence CC can be used to develop drugs for the treatment, prevention or delay of a neuronal disorder. In particular the newspan disorder.	Alzheimer's disease. The present sequence is the C. elegans sel-12 promoter.	<pre>\$ \$ Sequence 4137 BP; 1252 A; 770 C; 703 G; 1412 T; 0 other;</pre>	Query Match 42.1%; Score 631; DB 24; Length 4137; Best Local Similarity 83.3%; Pred. No. 6.7e-135; Matches 822; Conservative 0; Mismatches 10; Indels 155; Gaps 3;	OY     267 ACTATCACATCCTTTTGTCCGGGAAACAGACAGTATCGTTGAGAAGGGATTGATGTCACT     3.26       IIII     IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	Oy 327 TGGAAATGCTCTCGTCATGTTGTGGGTCGTTCTGATGACACTTCTGCTGATTGTTT 386	TITIOI DE L'ACTION

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1059 GAAGGAGA-----CCCGGAAGCTCAAAGGAGAGTATCCAAAATTCCAAGTATAATGCAG 1113
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                                                                                         659 GGACTGTGTGGTTTGTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                                                                                                              779 CGGCGCTGATTTATTCGTCTGGAGTCATCCTACCCTACGTTCTTGTTACTGCAGTTGAAA
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                                                                                                                                                                                                   CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Human early onset Alzheimer's disease (EOAD) gene.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 179 TATTIGIGCCGGIGICACTAIGCAIGGCICIGGIIGIITITIACGAIGAACACGAITACGI
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                                                                                                                                                                                                                                                                                                                                                                                                                        A full-length cDNA (AAT59536) of the early onset Alzheimer's disease
                                                                                                                                                                                                                                                                                                                                                                                                                                    Polypeptide (AAM1839). Another full-length cDNA (AAT59535) of the Polypeptide (AAM1839). Another full-length cDNA (AAT59535) of the Sequence cades for a 467-amino acid polypeptide (AAM1840). The 2 sequences can be used to generate primers and probes for the diagnosis of predisposition to Alzheimer's disease, esp. EOAD. They can also be used for prodn. of EOAD polypeptides in transformed host cells, and antisense sequences can be used for the treatment of EOAD.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Length 1750;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          40;
                                                                                                                                                                                                                                                                                                                                                       Early onset Alzheimer's disease gene - useful for diagnosing pre-disposition to Alzheimer's disease
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thes 512; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 1750 BP; 442 A; 389 C; 430 G; 478 T; 11 other;
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Pred. No. 1.4e-
0; Mismatches
                                                                                                          /note= "splice site"
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174..1565
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Matches 667; Conserv
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  Homo sapiens
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13-JUL-1995;
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                                                                                                                                                                                                                      CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAAAGGAGCCAATTTTCC
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ACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGAACAGT
                                  784 ATTTTGGTGTGGGGAATGATTTCCATTCACTGGAAAGGTCCACTTCGACTCCAGCAGG
                                                                                        GGACTGTGTGTGTGTTTTTTTTTTTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                                                                                                                  CGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTGAAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      TATTIGIGCCGGIGICACTAIGCAIGGCICTGGIIGITTIACGAIGAACACGAITACGI
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                                                                                                                                                                                                                                                                                                                                                                                                                                                         - useful for diagnosing
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Pred. No. 1.4e-47;
0; Mismatches 512; Indels
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                                            /*tag= a
249..260
/*tag= b
/label= VRSQ
/note= "splice variant"
                                                                                                                                                                                                                                                                                                                                                                                                                                                      Early onset Alzheimer's disease gene-
pre-disposition to Alzheimer's disease
         Location/Qualiflers
174..1577
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al Similarity 54.7%;
667; Conservative
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95US-0001142
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GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG

TTCTGATGACAGTTCTGCTGATTGTTTTCTATAAATACAAGTTTTATAAGCTTATTCATG

us-09-043-944-5.rng

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tumour antigen;
III; HUPF-1;
neurofilament-F; presenilin I; presenilin II; cellular tumour antigen glial fibrillary acidic protein; GFAP; p53; semaphorin III; HUPF-1; bcl-2; B-cell leukemia/lymphoma 2 proto-oncogene; HMGP-C; NSP-A; high mobility group protein-C; neuroendocrine specific protein A; ss.
                                                                                                                                                                                                                               Diagnosing disease by detecting frameshift mutations in RNA or corresponding protein mutations - used to diagnose cancer and neurological diseases, particularly Alzheimer's disease, and also for treatment and prevention with specific ribozymes or wild-type
                                                                                                                                                                                             Van Leeuwen FW;
                                                                                                                                                                SCI
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                                                                                                                                                                                                                                                                                        Disclosure; Figure 10; 258pp; English.
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                                                                                                                                                              ROYAL NETHERLANDS
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                                                   Homo sapiens
                                                                      WO9845322-A2
                                                                                                                                                                                         Burbach JPH,
                                                                                                            02-APR-1998;
                                                                                                                                10-APR-1997;
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This invention describes a novel method for the diagnosis of a disease caused by, or associated with, an RNA molecule that has a frameshift caused by, or associated with, an RNA molecule that has a frameshift cautation. The method is used to diagnose age-related diseases, contained the sepecially cancer and a wide range of neurodegenerative disorders (e.g. Alzheimer's disease, multiple sclerosis, alcoholic liver disease, diabetes mellitus cype II and many others listed) or susceptibility to these disorders. The method allows a definitive diagnosis of Alzheimer's disease in living companies, at an early stage. It is based on the observation that disease companies the used of neuronal system RNA molecules, specifically controlled by mutations in RNA rather than DNA. The invention for microtubule associated protein (beta-App), the collopoprotein E, microtubule associated protein (depaper) controllament-L, neurofilament-B, neurofilament-E, neurofilament-L, neurofilament-E, neurofilament-M, neurofilament-E, presentin I. (GRAP), the cellular controllament in the protein (GRAP), the cellular controllament in the protein (GRAP), the cellular controllament specific protein (GRAP), the cellular controllament specific protein A. This sequence encodes the wild type controllament protein fragments represented in AAY20854-Y20895. 301 299 GTATCGTTGAGAAGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGGGGGG 358 119 AAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATC TATTTGTGCCGGTGTCACTATGCATGGCTCTGGTTGTTTTACGATGAACACGATTACGT TTTATAGTCAAAACAATGGAAGGCATTTACTATCACATCCTTTTGTCCGGGAAACAGACA Gaps 40; Score 248.2; DB 19; Length 1392; Pred. No. 3.1e-47; Mismatches 513; Indels Sequence 1392 BP; 359 A; 310 C; 333 G; 390 T; 0 other; ; 0 16.5%; Conservative Similarity :999 Query Match 182 242 179 239 Local Best Loca Matches

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AAGTGTTTAAAAACCTATAACGTTGCTGTGGACTACATTACTGTTGCACTCCTGATCTGGA
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                                                                                                                        CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCC
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BP. AAX90184 standard; DNA; 1404 us-09-043-944-5.rng

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1019 AACGGGAGCTAGCTGCTGAGACCAACTGTACAAGACGCCAATTTTCACAGGCACGAAG 1078
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                                                                     551 AAGTGTTTAAAACCTATAACGTTGCTGTGGACTACATTACTGTTGCACTCCTGATCTGGA
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                                          GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         The present invention describes a gene mutant animal having a non-human mutant presentlin gene. The mutant presentlin gene causes amino acid substitutions at 1 or more positions of 79, 82, 96, 115, 120, 135, 139, 146, 163, 280, 281, 281, 282, 286, 283, 284, 267, 269, 280, 285, 286, 290, 318, 384, 392, 410, 426 and 436, with corresponding replacing isoleucine of position 213 by another amino-acid especially replacing isoleucine of position 213 by another amino-acid especially replacing isoleucine of position 213 by another amino-acid especially replacing isoleucine of position 213 by another amino-acid especially replacing isoleucine of position 213 by another amino-acid especially replacing for the study of human Alzheimer's diseases and to screen and evaluate substances as candidates for prevention and/or therapy of letter presenting of pering of patients. They can over-produce amyloid beta protein by the presentlining of such ologically close to human patients with Alzheimer's diseases. The present sequence encodes human presentlining in the present
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              TTCTGATGACAGTTCTGCTGATTGTTTTCTATAAATACAAGTTTTATAAGCTTATTCATG 418
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               179 TATTIGIGCCGGIGICACIAIGCAIGGCICIGGIIGITITIACGAIGAACACGAÍAACGI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          TTTATAGTCAAAACAATGGAAGGCATTTACTATCACATCCTTTTGTCCGGGAAACAGACA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Mutant presentlin-1 gene-introduced animals, useful as model animals for study of Alzheimer's diseases in human and screening substances for prevention and/or treatment of the diseases
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                                                                                                                                        Presenilin-1; mutation; gene mutant animal; Alzheimer's disease;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          16.5%; Score 248.2; DB 20; Length 1404; 54.6%; Pred. No. 3.1e-47; ive 0; Mismatches 513; Indels 40;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence 1404 BP; 362 A; 312 C; 337 G; 393 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Disclosure; Page 53-54; 64pp; Japanese.
                                                                                               presenilin-1 encoding DNA
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                                                                                                                                                                                    Homo sapiens
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NF-kappa B; neuronal degeneration; spinal muscular atrophy; paralysis; peripheral neuropathy; motorneuron disorder; neurodegenerative disorder; Parkinson's disease; Meniere's disease; multiple sclerosis; Bell's palsy; Huntington's chorea; Down's syndrome; amyotrophic lateral sclerosis; Alsy, nerve deafness; Alzheimer's disease; epilepsy; ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           The invention relates to human Par-4 protein, presentiin protein (PSI and PS2) and their corresponding DNA molecules. The invention also relates to a method for identifying inhibitors of neuronal degeneration, comprising cotransfecting eukaryotic host cells expressing presentlin exposing the cotransfected cells to a candidate molecule and monitoring the ability of the candidate molecule to induce NF-kappa B activation. Presentlin proteins participates in nuclear factor kappa B (NF-kappa B) signalling and activation. The inhibitors of neuronal degeneration are useful for treating neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's syndrome, nerve deafness, Meniere's disease and also for
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       treating peripheral neuropathies, motorneuron disorders such as amyotrophic lateral sclerosis (ALS), Bell's palsy and various conditions involving spinal muscular atrophy and paralysis. The present DNA sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Identifying inhibitors of neuronal degeneration useful for treating e.g. Alzheimer's disease, by determining the ability of a compound induce nuclear factor kappa B activation, with the involvement of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     /*tag= a
/product= "Human presenilin PS1 protein"
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04-JAN-2001; 2001US-0754949
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54.6%;
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Pred. No. 3.1e-47;
0; Mismatches 513;
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                                          GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG
                                                                                         GGACTGTGTGGTTTGTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
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    useful for
Alzheimer's

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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Identifying genes which cause improper chromosome segregation, screening for inhibitors of chromosome missegregation and processes caused by genes encoding chromosome missegregation promoters was exemplified using Alzheimer's disease. The sequences given in AAT87401 to AAT87426 can be used in the above methods.
                                                                                                                                                      AD3; AD4/AD3LP; Alzheimer's disease; chromosome; missegregation;
presenilin; inhibitor; AD; trisomy 21; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Score 248.2; DB 18; Length 1488;
Pred. No. 3.2e-47;
0; Mismatches 513; Indels 40;
                                                                                                                                                                                                                                                                                                                                                                                                                                                              missegregation
diseases, e.g.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                         Identifying genes which cause chromosome identifying causes of and treatments for
                                                                                                                                                                                                                 Location/Qualifiers
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/note= "C-terminal"
 1361 AGCCTTTTATGGACCAATT 1379
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                                                         AAT87402 standard; DNA; 1488
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Best Local Similarity 54.6%;
Matches 666; Conservative
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   disease, cancer and ageing
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                                                                                                                              Partial AD3 sequence.
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                                                                                                                                                                                                                                                                                                                                                                                                                                    P-PSDB; AAW28507.
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                                                                                                                                                                                            Homo sapiens
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                                                                                AAT87402;
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                                                                                                                                                                                                                                                                                                                                                                                                                                           This sequence encodes the PSI/429 presentlin peptide (II) of the invention. Cells transformed with the DNA are used to produce recombinant and analoques, useful e.g. as immunogens for generating an immune response against PSI/429 (II) is a new product of the PSI gene.

To response against PSI/429 (II) is a new product of the PSI gene.

The nucleic acids are generally useful as probes for detection and quantification of PSI/429, particularly for diagnosis of AD, especially the target sequences that particularly for diagnosis of AD, especially the target sequences that hybridise with probes are isolated for sequencing. Antibodies (Ab) can also be used to identify epitopes and for affinity purification of peptides. Antisense nucleic acid may also be used to regulate expression of the PSI/429 gene, and both nucleic acids and peptides are useful as size markers in electrophoresis, chromatography etc. The transgenic animals are used as models for AD, e.g. for testing drugs. Regulators of involving mitochondrial pathology, apoptosis and neurodegeneration.

Typical regulators are antisense sequences, ribozymes, aptamers, coding sequences to particular cellular locations.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      TITATAGTCAAAACAATGGAAGGCATTTACTATCACATCCTTTTGTCCGGGAAACAGACA 298
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                                                           Presenilin peptide; PS1/429; immunogen; immune response; PS1 gene;
Alzheimer's disease; mitochondrial pathology; neurodegeneration;
                                                                                                                                                                                                                                                                                                                                                                                    DNA encoding presentlin peptide PSI/429 and its analogues - useful for diagnosis and treatment of Alzheimer's disease
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      16.5%; Score 248.2; DB 19; Length 1703; 54.6%; Pred. No. 3.3e-47; Live 0; Mismatches 513; Indels 40;
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                                                                                                                                       Location/Qualifiers
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                                    PS1/429 protein coding sequence.
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96US-0659296.
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                                                                                                                                                                                                                                                                                                                          Davis JN,
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P-PSDB; AAW41429.
                                                                                                                                                                                                                                                                                                (FARB ) BAYER CORP.
                                                                                     apoptosis; ss.
                                                                                                             Homo sapiens.
                                                                                                                                                                                                                                                                                                                       Chisholm JC,
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06-JUN-1996;
            04-JUN-1998
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GTATCGTTGAGAAGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCG
                     TICTGATGACAGTTCTGCTGATTGTTTCTATAAATACAAGTTTTATAAGCTTATTCATG
                                                                                                                                  GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG
                                                                                                                                                                                                                            839 ACACGACAGACCCCGTGAACCGACGTCGTCAGACTCAAATACTTCTACAGCTTTTCCTG
                                                                                                                                                                    AAGTICTGAAAAGTITCGATGTGTCTCCCAGCGCACTAITGGTTTTGTTTGGACTGGGTA
                                                                                                                                                                                                                                                                        ACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGT
                                                                                                                                                                                                                                                                                                                                        GGACTGTGTGGTTTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                            CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAAACGAGCCAATTTTCC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                CGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTGAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              888 CAGCTCTCATTTACTCCTCAACAAT-----GGTGTGGTTGGTGAATATGGCA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    1079 AGGAAGAGAGGTGTGAAACTTGGTCTGGGCGACTTCATTTTCTACTCTCTCCTCG
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538 858 658 978 718 778

838

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1039 CGAAAGGTCCACTTGGTATGCTGGTTGAAACAGCTCAGGAGAAAATGAAACGCTTTTTC 1098
                                                                                                                                                                                                                                                                                                               1201 AAAGCACAAAAGGGAGTC--ACAAGACACTGTTGCAGAGAATGATGGCGGGTTCAG 1258
                                                                                                                                                                                                                                                                                                                                                                                                                                                  959 AAGTGCAAATCGAATACTACAGCTTCAACGACAAAACTCTGGAGTAAGGGTGG 1018
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                                                                        799 AAGTGTTTAAAACCTATAACGTTGCTGTGGACTACATTACTGTTGCACTCCTGATCTGGA
                                                                                                  ACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAAACAT
                                                                                                                                                                1146 GAAGGAGA-----CCCGGAAGCTCAAAGGAGTATCCAAAAATTCCAAGTATAATGCAG
                                                                                                                                                                                                                                                                                                                                                                                                 899 GAGAGGCGAGTTGTTCATCTGAAACGCCAAAACGGCCAAAAGTGGAAACGAATTCCTCAAA
   GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG
                                                                                                                          ATTTTGGTGGTGGGAATGATTTCCATTCACTGGAAAGGTCCACTTCGACTCCAGCAGG
                                                                                                                                                 GGACTGTGTGTTTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                                                                                                                                                                                                  719 CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCC
                                                                                                                                                                                                                                                                                                  779 CGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTGAAA
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                          AAGTTCTGAAAAGTTTCGATGTCTCCCAGCGCACTATTGGTTTTGTTTTGGACTGGGTA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  nseq
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    - used for
                                                                                                                    PS-1; presenilin; presenilin-1; PSP-1; Alzheimer's disease; serine protease; neurodegeneration; predisposition; diagnosis;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         The sequence is that of encoding the presenllin PS-1 which was in the cloning and isolation of the serine protease PSP1.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Length 2764;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    40;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      16.5%; Score 248.2; DB 19; Length 54.6%; Pred. No. 3.8e-47; ive 0; Mismatches 513; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Nucleic acids encoding human serum protease protein(s) diagnosing pre-disposition to Alzheimer's disease, etc
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Sequence 2764 BP; 715 A; 623 C; 652 G; 773 T; 1 other;
                                                                                                                                                                                                                                                                                                                                                                                                             Karran EH;
                                                                                                                                                                                                                                                                                                                                                                                                         Browne MJ, Clinkenbeard HE, Creasy CL,
Livi GP, Southan CD;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Example 1; Page 24-25; 65pp; English.
                                                                                                                                                                                  Location/Qualifiers
249..1652
/*tag= a
/product= PS-1
                        BP.
                                                                                                                                                                                                                                                                                                                                                                    (SMIK ) SMITHKLINE BEECHAM CORP. (SMIK ) SMITHKLINE BEECHAM PLC.
                    AAV29525 standard; cDNA; 2764
                                                                                                                                                                                                                                                                                                                     96us-0032875.
96us-0025436.
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Matches 666; Conservative
                                                                                              PS-1 cDNA.
                                                                                                                                                                                                                                                                                                                                                                                                                                             WPI; 1998-161101/15.
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                                                                                              Homo sapiens
                                                                                                                                                          Homo sapiens
                                                                                                                                                                                                                                                                                             26-AUG-1997;
                                                                      13-0CT-1998
                                                                                                                                                                                                                                                                                                                    13-DEC-1996;
06-SEP-1996;
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                                                                                                                                                                                                                                                                     11-MAR-1998
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                                              AAV29525;
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1200

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This sequence encodes the PSI/467 presentlin peptide. This sequence is specifically stated as not being in the nucleic acid of the invention, which encodes the PSI/429 presentlin peptide PSI/429 (II). Cells transformed with the DNA are used to produce recombinant (II) and analogues, useful e.g. as immunogens for generating an immune response against PSI/429. (II) is a new product of the PSI gene, mutations in which cause Alzheimer's disease (AD). The nucleic acids are generally useful as probes for detection and quantification of PSI/429, particularly for diagnosis of AD, especially the target sequences that puricularly for diagnosis of AD, especially the target sequences that hybridise with probes are isolated for sequencing. Antibodies (Ab) can also be used to identify epitopes and for affinity purification of peptides. Antisense nucleic acid may also be used to regulate expression of the PSI/429 gene, and both nucleic acids and peptides are useful as animals are used as models for AD, e.g. for testing drugs. Regulators of the PSI/429 gene or polypeptide can be used to treat e.g. AD or diseases involving mitochondrial pathology, apoptosis and neurodegeneration.

Typical regulators are antisense sequences, ribozymes, aptemers, synthetic or natural compounds. (II) may also be used to target other conding sequences to particular cellular locations.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                239 TTTATAGTCAAAACAATGGAAGGCATTTACTATCACATCTTTTGTCCGGGAAACAGACA 298
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     encoding presentlin peptide PSI/429 and its analogues - useful diagnosis and treatment of Alzheimer's disease
                                                                                               Presentlin peptide; PS1/429; immunogen; immune response; PS1 gen. Alzheimer's disease; mitochondrial pathology; neurodegeneration;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          16.5%; Score 248.2; DB 19; Length 2764; 54.6%; Pred. No. 3.8e-47; 1ve 0; Mismatches 513; Indels 40;
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                                                                                                                                                                                                                                                                                                Location/Qualifiers
249..1652
/*tag= a
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                                     protein coding sequence.
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96US-0659296.
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Matches 666; Conservative
                                                                                                                                                                   apoptosis; PS1/467; ss
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                                                                                                                                                                                                                                   Homo sapiens
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06-JUN-1996;
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                                                                                                                                                                                                                                                                                                                                                                                                                           WO9746678-A1
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NAME OF THE PARTY 
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               419 GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG
                                                                                                                                799 AAGTGTTTAAAACCTATAACGTTGCTGTGGACTACATTACTGTTGCACTCCTGGA
                                                                                                                                                                                                              539 ACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGT
                                                                                                                                                                                                                               659 GGACTGTGTGTTTGTTTTTTTTTTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                                                                                                                                                                                                                                                                                       CGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTGAAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The present invention relates to DNA molecules comprising the promoter of the sel-12 gene from Caenorhabditis elegans operably linked to a heterologous DNA sequence encoding a protein of interest. The sequence can be used to develop drugs for the treatment, prevention or delay of neuronal disorder. In particular, the neuronal disorder may be familial Alzheimer's disease. The present sequence is a presentin coding sequence described in the exemplification of the invention.
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                                                                                                                                                                                                                                                                                          Sel-12; presenilin; neuronal disorder; familial Alzheimer's disease; amyloid precursor protein; APP; ds.
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                                                           CTGTGGGCCAGAGCCCTGCACTCAATTCTGAATGCTGCCATCATGATCAGTGTCATTG
         TTTATACCCGGAAGGATG---GGCAGCTAATCTATACCCCATTCACAGAAGATACCGAGA
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different forms of wild type human presentiin-1 (PS-1). The form
C represented by AAT40029 results from alternate splicing of the genomic
DNA sequence. AAT40031 represents the coding sequence for wild type human
C PS-2. The presentlins are a family of highly conserved integral membrane
C proteins with a common structural motif, common alternate splicing
D patterns, and common mutational hot spot regions. Nutredions in PS genes
C are implicated in familial Alzheimer's disease (AD) and possibly other
C diseases such as cerebral haemorrhage, schizophrenia, depression etc., so
these diseases. The encoded proteins, or vectors that express them or
C containing antisense sequences, antibodies selective for mutant forms of
C the encoded proteins (such as AAW05736) and modulators of PS gene
C containing are potentially useful for treatment of AD etc. Transgenic
C animals are useful as models for drug screening. The antibodies can also
C be used e.g. for affinity purification and in immunoassays.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          119 AAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATC 178
                                                                                                protein; AD;
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                                                                                        Presenilin-1; human; hPS1-1; hPS1-2; PS-2; integral membrane prote: familial Alzheimer's disease; cerebral haemorrhage; schizophrenia; depression; antibody; gene expression modulator; therapy; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          New presentlin genes - useful for diagnosis, therapy and drug screening of familial Alzhelmer's disease, cerebral disorders, etc.
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Pred. No. 3.8e-47;
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                                                        Presenilin-1-1 wild type coding sequence.
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95US-0496841.
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al Similarity 54.6%;
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652 G; 772 T; 1 other;

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Sequence 2765 BP; 715 A; 625

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Chromosome 14 early-onset familial Alzheimer's disease gene PSI mutants - useful for diagnosing likelihood of developing Alzheimer's disease, also anti-sense sequences, antibodies and vaccines to delay
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this position"
                                                                   Mutant; antisense; antibody; vaccine; Alzheimer's disease;
                                                    Human S182 gene, PS1 locus, related to Alzheimer's disease
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The present sequence represents the human S182 gene, PS1 locus. Mutant PS1 produces a gene product that increases the probability of Alzheimer's disease. Possible mutations of the PS1 locus are shown in the features table. A nucleic acid sequence able to hybridise to sequences coding for a mutant PS1 polypeptide can be used as probes for diagnosing an increased likelihood of contracting Alzheimer's disease. Antibodies against the mutant polypeptide can also be used for this purpose. Vectors containing or expressing a nucleic acid molecule, protein or antibody specific for mutant PS1 can be administered to a

patient to reduce the likelihood, or delay the onset, of Alzheimer's disease, e.g. anti-sense RNA expression can be used to decrease expression of the RSI peptide. Transgenic animals expressing the Alzheimer's disease protein can be used to test candidate therapeutics and to investigate the normal role of PSI. The PSI peptide may also be included in pharmaceutical compositions (vaccines) for Alzheimer's

disease therapy

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                                 Gaps
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    Length 2765;
                              Indels
    DB 18;
 Score 248.2; DB 18;
Pred. No. 3.8e-47;
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Query Match 16.5%;
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variation 324335 /*tag=.n /*note= "deletion of exon 4 by a val6-Gln-2 function) variation 10181116 /*tag= 0 /note= "absence of	492 /*tag= /note=	mutation 591 /*tag= /note= mutation 664	/*tag= /note= mutation 676 /*tag=	/note= "T to C FAD mutation site 684 /* tag= t	/note= " mutation 736	A to G FAD mutation site	mutation 985		mutation	` ` `	וותרמרוסוו	<pre>mutation 1104 /*tag= aa //note= "C to G FAD mutation site</pre>		FT //tag= ac FT //tag= ac FT //note= "C to G FAD mutation site (Leu392Val)" FT mutation 1477	mutation	,		PD 15-JAN-1998. XX PF 04-JUL-1997; 97WO-CA00475.	-JAN-1997; -JUL-1996;	12-JUL-1 08-NOV-1	PA (HSCR-) HSC RES 6 DEV LP. PA (UTOR) UNIV TORONTO GOVERNING COUNCIL.
	1549	Db 1609 AGCCTTTTATGGACCAATT 1627 RESULT 15	AAVO4666 ID AAVO4666 standard; cDNA; 2765 BP. XX AC AAVO4666:			<pre>KW Presenlin-1; PS1 gene; human; familial Alzheimer's disease; FAD; KW cerebral haemorrhage; schizophrenia; depression; epilepsy; KM mental retardation; diagnosis; therapy; transgenic animal; ss.</pre>	nomo saprens.	Key CDS	uoxa	FT exon 114195	F1 cxon 196.335 FT cxon 146.335 FT /tag= d	FT	exon	FT exon 729796 FT	FT exon 7971017  FT /*tag= h  FT /number= 8	exon 1018.1111 /*tag= 1	exon	FT /number 10	exon 137814	FT	/numper-

us-09-043-944-5.rng

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presentlin-1 (PS-1) protein DNA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Alzhelmer's disease (FAD) and may be causative of other disorders, cognitive, intellectual, neurological or physiological disorders such as cerebral haemorrhage, schizophrenia, depression, mental retardation and epilepsy. Isolation of the hPSI cDNA collowed genetic mapping of the AD3 region at 14924.3, construction of a physical contig spanning the AD3 region, transcription mapping and analysis of candidate genes, and recovery of candidate genes by the PPR from brain mRNA. In this cDNA, exon 1 is spliced directly to exon 3. Other hPS1 sequences (see also AAV04667) result from alternative splicing of the mRNA transcript. A mouse PS1 homologue also provided, as well as genomic sequences for hPS1 (see AAV04668) and a human presentine sequence for hPS1 (see AAV04669) are also provided, as well as genomic sequences for hPS1 (see AAV04667). Use of the nucleic acids and proteins comprising or FAD, identifying and developing therapeutics for treatment of FAD, and in producing one lines and transgenic animals useful as models of FAD, interaction are also provided.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          This cDNA clone, deposited as ATCC 97124, codes for human presenilin-1 (hPS1, see AAW23964). Mutations in the presenilin genes have been linked to the development in humans of forms of familial
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATC
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                                                                                 New isolated mutant presentlin-1 genes - useful for developing products for use in detection, diagnosis and therapy of Alzheimer'
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              DB 19; Length 2765;
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Pred. No. 3.8e-47;
0; Mismatches 513; Indels
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              PH;
             St George-Hyslop
                                                                                                                                      Disclosure; Page 178-180; 238pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                    interacting proteins are also provided.
                                                                                                             disease and for drug screening
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Best Local Similarity 54.6%;
Matches 666; Conservative (
             Fraser PE, Rommens JM,
                                         WPI; 1998-286355/25
                                                      P-PSDB; AAW23964
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                                                                                                                                                                                             899 GAGAGGCGAGTTGTTCATCTGAAACGCCAAAACGGCCAAAAGTGAAACGAATTCCTCAAA
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919 CATAICTCATIATGAITAGTGCCCTCATGGCCCTGGTGTTATCAAGTACCTCCCTGAAT
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                                                      GGACTGTGTGTTTGTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
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658 978 718 1098

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1146 GAAGGAGA-----CCCGGAAGCTCAAAGGAGGTATCCAAAATTCCAAGTATAATGCAG 1200
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         859 ATTITGGTGGGGGAATGATTICCATTCACTGGAAAGGTCCACTTCGACTCCAGCAGG 918
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/product= "presenilin
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                                                                                                                                                                                                                                                                                                                  The invention relates to a method for identifying modulators of presentlin and catenin p120. Modulators of catenin p120 and presentlin are useful for the treatment and prophylaxis of disorders that is responsive to modulation of presentlin/catenin p120 activity. In particular, neuronal disorders such as cognitive disorders and neurodegenerative diseases such as Alzheimer's disease. Catenin p120 DNAS are useful for identifying mutations in catenin p120 genes. Guentification of such mutations assist in the diagnosis of or succeptibility to Alzheimer's or other conditions associated with p120 DNAS are also used in hybidisation studies to monitor expression of expression. The present DNA sequence encodes human presentlin-1 (PS-1)
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                                                                                                                                                                                                                     Identifying presentlin or catenin p120 activity modulator useful for modulating presentlin-catenin p120 interaction and thus for treating cognitive disorder e.g., Alzheimer's disease comprises enhancing cognitive function
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  TTCTGATGACAGTTCTGCTGATTGTTTTCTATAAATACAAGTTTTATAAGCTTATTCATG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            40;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Score 248.2; DB 22; Length
Pred. No. 3.8e-47;
0; Mismatches 513; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Sequence 2765 BP; 715 A; 624 C; 652 G; 773 T; 1 other;
                                                                                                                                                                                                                                                                                         Example 1; Page 43-45; 48pp; English.
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                                                        09-MAR-2001; 2001WO-GB01059
                                                                                     .0-MAR-2000; 2000GB-0005895
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Best Local Similarity 54.6
Matches 666; Conservative
                                                                                                                   (GLAX ) GLAXO GROUP
                                                                                                                                                Rowley A,
                                                                                                                                                                            2001-589954/66
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                              13-SEP-2001
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                                                                                                                                                                                                                                           Identifying a modulator of presentlin function by determining the ability of presentlin to bind to a K1AA0253 polypeptide in the presence and absence of a test compound, useful in the treatment or prophylaxis.
                                                                                                                                                                                                                                                                                                                                                      The present sequence encodes human presentlin 1. KIAA0253 binds to presentlin. The specification describes a method of identifying a modulator of presentlin function or KIAA0235 function. The method comprises determining presentlin activity or KIAA0253 activity in the presence and absence of a test compound, where presentlin activity is determined by its ability to bind to KIAA0253. A modulator of presentlin or KIAA0253 polypeptide is useful in the manufacture of a medicament for the treatment or prophylaxis of Alzheimer's disease. The KIAA0253 polypucleotide and KIAA0253 polypeptide are useful in the treatment, prophylaxis or diagnosis of Alzheimer's disease.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      AAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    AAGATGAGGAAGAAGATGAGCTGACATTGAAATATGGCGCCAAGCATGTGATCATGC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              513; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 2765 BP; 715 A; 624 C; 652 G; 773 T; 1 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Score 248.2; DB 2;
Pred. No. 3.8e-47;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            0; Mismatches
                                                                                                                                                                                                                                                                                                                         Disclosure; Page 42-44; 48pp; English.
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                                                                                                                                                                  Blackstock
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54.6%;
                                                                          2001WO-GB01057
                                                                                                     10-MAR-2000; 2000GB-0005894
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         666; Conservative
                                                                                                                                                                                                                                                                                             Alzheimer's disease
                                                                                                                                    (GLAX ) GLAXO GROUP
                                                                                                                                                                    Rowley A,
                                                                                                                                                                                                 WPI; 2001-522960/57
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Similarity
                                                                                                                                                                                                                 P-PSDB; AAG63936
            WO200167109-A1
                                                                        09-MAR-2001;
                                           13-SEP-2001
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                                                                                                                                                                                                                                             1146 GAAGGAGA----CCCGGAAGCTCAAAGGAGATATCCAAAAATTCCAAGTATAATGCAG 1200
                                                                                                                                                                                                                                                                                                                                                                 1259 TGAGGAATGGGAAGCCCAGAGGGACAGTCATCTAGGGCCTCATCGCTCTACACCTGAGTC 1318
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Human; presentlin 1; PSI; amyloid precursor protein; APP; drug screening; Alzheimer's disease; Parkinson's disease; multiple sclerosis; stroke; Huntington's disease; amylotrophic lateral sclerosis; Picks disease; head injury disease; frontal lobe dementia; cerebellar degeneration;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                        959 AAGTGCAAATCGAATCGAATACTACAGCTTCAACGACACAAAACTCTGGAGTAAGGGTGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                GGACTGTGTGTTTGTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                    979 GGACTGCGTGGCTCATCTTGGCTGTATTTCAGTATATGATTTAGTGGCTGTTTTGTGTC
                                                                                                 CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCC
                                                                                                                                                          CGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTGAAA
                                                                                                                                                                                                                  ACACGACAGACCCCGTGAACCGACGTCGACACTCAAATACTTCTACAGCTTTTCCTG
                                                                                                                                                                                                                                                                          899 GAGAGGCGAGTTGTTCATCTGAAACGCCAAAACGGCCAAAAGTGAAACGAATTCCTCAAA
                                                                                                                                                                                                                                                                                                                                                                                             AACGGGAGCTAGCTGCTGAGAGACCAACTGTACAAGACGCCAATTTTCACAGGCACGAAG
                                                                                                                                                                                                                                                                                                                                                                                                                          1319 ACGAGCTGCTGTCCAGGAACTTTCCAGCAGTAT-------CCTCGCTGGTGAAGACC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 GCAAGGCTT-----CATCGTACTTTGACTGGAACACGACTATCGCTTGTTATGTGGCCCA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                       1079 AGGAAGAGAGGTGTGAAACTTGGTCTGGGCGACTTCATTTTCTACTCTGTTCTCCTCG
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                                                                                                                                                                           presentlin 1 (PS1) cDNA #1.
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The invention relates to mutant presentlin 1 (PSI) and presentlin 2 (PS2) polypeptides. Presentlin are involved in the processing of amyloid precursor protein (APP) from which major amyloidogenic peptides are cleaved. Mutant presentlins are useful for identifying agents that modulate amyloid beta-peptide (Abeta) derived peptide production. Mutant presentlin is also useful as a target for screening drugs useful in the protein processing, such as Alzheimer's disease, parkinson's disease, protein processing, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, Huntington's disease, amylotrophic lateral sclerosis, head injury disease, picks disease, frontal lobe dementia, cerebellar degeneration, stroke, ischaemic injury and schizophrenia. A transgenic non-human animal is useful for analysing the interaction between APP and mutant presentiin-processing protease in vivo, and for screening antimative mater for any and schizophremia and animal second and any and second and sec
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Novel isolated mutant presentlin 1 and presentlin 2 polypeptides, useful for screening of drugs for treating pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's
                                                                     /transl_except= (pos:772].774, aa:Xaa)
/transl_except= (pos:775..777, aa:Xaa)
/note= "Xaa corresponds to unknown amino acid"
                                                presenilin-1 protein"
                                         /product= "Human mutant
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Claim 44; Page 65; 80pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (PHAA ) PHARMACIA & UPJOHN CO.
                                                                                                                                                                                                                                                                                                                                 29-JUN-2001; 2001WO-US16508
                                                                                                                                                                                                                                                                                                                                                                                               30-JUN-2000; 2000US-215345P
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Tomasselli AG;
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P-PSDB; AAE17045.
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                                                                                                                                                                                                                                                                                                     430
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                                                                                      119 AAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATC
                                                                                                               AAGATGAGGAAGAATGAGGGGCTGACATTGAAATATGGCGCCCAAGCATGTGATCATGC
                                                                                                                                               TATITGIGCCGGIGTCACTAIGCAIGGCICTGGIIGIITITIACGAIGAACACGAITACGI
                                                                                                                                                                   TTCTGATGACAGTTCTGCTGATTGTTTTCTATAAATACAAGTTTTATAAGCTTATTCATG
                                                                                                                                                                                                                                                                                                                                           GATGGCTTATTGTCAGCAGTTTTCTTCTTTTCCTATTCACTACAATCTATGTGCAAG
                                                                    Gaps
                                                                 40;
                                 Score 247; DB 24; Length 1404;
Pred. No. 5.9e-47;
0; Mismatches 516; Indels 40.
Sequence 1404 BP; 361 A; 312 C; 335 G; 390 T; 6 other;
                                 16.5%;
54.4%;
                                                         663; Conservative
                                             Similarity
                              Query Match
                                                                                                                    194
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                   AAGTGTTTAAAAACCTATAAACGTTGCTGTGGACTACATAACTGTTGCACTCCTGATCTGGA
                                                                                                              AAGTICTGAAAAGTITCGATGTGTCTCCCAGCGCACTATTGGTTTTGTTTGGACTGGGTA
                                              ACTATGGAGTTCTCGGAATGATGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGT
                                                             839 ACACGACAGACCCCGTGAACCGACGTCGTCAGACTCAAATACTTCTACAGCTTTTCCTG
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      GGACTGCGTGGCTCTTTGGCTGTGTTTTCAGTATATGATTTAGTGGCTGTTTTGTGTC
                                                                                                                                                                                                                                                                     719 CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCC
                                                                                             ACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGT
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                                                                                                                                                     839 ACACGACAGACCCCCGTGAACCGACGTCGTCAGACTCAAATACTTCTACAGCTTTTCCTG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                    An S182 gene cDNA clone (AAT63207), deposited as ATCC 97238, was isolated from a human brain library. Several mutations in the S182 gene have been found in families with members affected by early onset Alzheimer's disease (AD): in 2 families Met to Val at 142; in 1 family Pro to Ser at 263; in 4 families Glu to Ala at 276; and in 1 family Glu to Gly at 280. In all cases the mutations were detected only in affected family members. Detection of the mutations, e.g. by PCR (see also AAT63208-13), is used to diagnose AD, or a predisposition to it. Transgenic assessing potential drugs. Probes based on the gene can be used to identify homologues of S182, e.g. one present on human chromosome 1 which may be associated with AD in some families.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             179 TATITGIGCCGGIGICACTAIGCAIGGCICIGGIIGITITITACGAIGAACACGAIIACGI
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Gaps
                                                                                                                                                                                                                                                                                                                                                                   disease - and related protein and transgenic animals, useful as models for screening and assessing potential drugs
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            16.4%; Score 246.6; DB 18; Length 1911; ilarity 54.6%; Pred. No. 7.9e-47; Conservative 0; Mismatches 514; Indels 40;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              40;
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                                                                                                                                                                                                                                                                                                                                                                  New mutants of the S182 gene associated with familial
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(UNIW ) UNIV WASHINGTON SCHOOL MED.
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 transgenic animal;
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                              Homo sapiens
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18-JUL-1995;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Identifying susceptibility to a neurological disease, comprises detecting an alternative splice site in a polyadenylated mRNA transcript in a sample of genetic material, where the alternative. Splice site encodes AAW22944, or detecting AAW22944 in the protein encoded by the mRNA. Tests on 3 early onset familial Alzheimer's disease (FAD) patients and 4 neurologically normal subjects, indicated that mRNA transcripts of the presentin 1 gene in samples from various brain regions occur in 2 forms, PS-1-long (containing a VRSQ motif, and PS-1-short (lacking the VRSQ motif, i.e. the protein encoded by the present sequence), and that the PS-1-long levels in hippocampus and frontal cortex samples are significantly lower in FAD patients than in AD and normal subjects.
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 Identification; determination; neurological disease susceptibility; detection; alternative splice site; polyadenylated mRNA transcript; familial Alzheimer's disease; FAD; presenilin 1; VRSQ variant; ss.
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(UYSF-) UNIV SOUTH FLORIDA DEPT PSYCHIATRY
(UNIW ) UNIV WASHINGTON.
                                                                                             Location/Qualifiers
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                                                              Homo sapiens
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Human; ss; granulocytic cell; DNA chip; bacterial infection; viral infection; parasitic infection; protozoal infection; fungal infection; sterile inflammatory disease; psoriasis; rheumatoid arthritis; glomerulonephritis; asthma; thrombosis; cardiac reperfusion injury; renal reperfusion injury; ARDS; adult respiratory distress syndrome; inflammatory bowel disease; crohn's distress; ulcerative colitis; periodontal disease; granulocyte activation; chronic inflammation; allergy. Human cDNA differentially expressed in granulocytic cells #483.

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Homo sapiens.

WO200228999-A2.

11-APR-2002.

03-OCT-2001; 2001WO-US30821.

03-OCT-2000; 2000US-237189P.

(GENE-) GENE LOGIC INC.

Vockley J; Beazer-Barclay Y, Weissman SM, Yamaga S,

WPI; 2002-435328/46.

Detecting granulocyte activation by detecting differential expression of genes associated with granulocyte activation, which serves as diagnostic markers that is useful for monitoring disease states and drug toxicity

Claim 1; SEQ ID No 483; 114pp; English.

The invention relates to detecting (MI) granulocyte (GC) activation (GCA), by detecting the level of expression of gene(s) (GS) identified by CGA, by detecting the level of expression of gene(s) (GS) identified by the analysis as given in the specification, and comparing the expression level to an acpression level in an unactivated of the expression level in an unactivated of the expression of GS is indicative of GCA. Also included are modulating (M2) GA by contacting GC with an agent that alters the expression of at least one gene in GS; (2) screening (M3) for an agent capable of modulating (GA) or an inflammation (especially choosing) in a tissue, an allergic response in a subject, exposure of a subject to a pathogen or sterile inflammatory disease using the chronic) in a tissue, an allergic response in a subject, exposure of a subject to a pathogen or sterile inflammatory disease, by detecting the level of expression of the gene is indicative of inflammation.

CC (4) treating (M3) an inflammation (especially chronic) or in a tissue, an allergic response in a subject, exposure of a subject to a pathogen or sterile inflammation disease, by contacting a tissue having confidence of inflammatory disease, by contacting a tissue having the inflammation with an agent that modulates the expression of gene(s) from GS in the tissue. MI is useful for detecting GCA, M2 is useful for modulating GA, M3 is useful for recentle of modulating or sterile inflammation in a tissue, M4 is useful for recentle of modulating or sterile inflammation in a shorter to a mathogen or sterile inflammation and subject to a nathogen or sterile inflammation and an inflammation in a tissue, M3 is useful for recentle GCA preferably in an inflammation in a tissue, M3 is useful for steerile mathoden or sterile inflammation and subject to a sub glomerulonephritis, asthma, thrombosis, cardiac reperfusion injury, renal reperfusion injury, ARDS, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, periodontal disease; also bacterial infection, viral infection, parasitic infection, protozoal infection, fungal infection and MS is useful for treating one of the above conditions. The present response in a subject, exposure of a subject to a pathogen or sterile inflammatory disease (e.g. psoriasis, rheumatoid arthritis, useful for treating one of the above conditions. The present sequence represents a gene differentially expressed in granulocytes. On the perinted specification. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic ormat directly from WIPO at ftp.wipo.int/pub/published\_pct\_sequences. 

Sequence 3056 BP; 762 A; 688 C; 740 G; 866 T; 0 other;

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                                  TTCTTATCGGTCTCTGCTTCACTCTTGTCCTGCTCGCCGTCTTCAAACGAGCACTCCCGG
                                                    TATTAATTGGTTTGTGCCTTACATTATTACTCCTTGCCATTTTCAAGAÄAGCATTGCCAG
                                                                                                                                                                                                                                                                                                Presentlin-1; human; hPS1-1; hPS1-2; PS-2; integral membrane protein; familial Alzheimer's disease; cerebral haemorrhage; schizophrenia; depression; antibody; gene expression modulator; therapy; ss.
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(UTOR ) UNIV TORONTO GOVERNING COUNCIL.
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P-PSDB; AAW05734
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expression are potentially useful for treatment of AD etc. Transgenic animals are useful as models for drug screening. The antibodies can also be used e.g. for affinity purification and in immunoassays.
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                                                                                                                     DB 17; Length 3086;
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                                                                                                                                                           0; Mismatches 514; Indels
                                                                             Sequence 3086 BP; 789 A; 688 C; 740 G; 866 T; 3 other;
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                                                                                                                     Score 246.6;
Pred. No. 9.1
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54.6%;
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    1079 AGGAAGAGAGGTGTGAAACTTGGTCTGGCGACTTCATTTTCTACTCTGTTCTCCTCG
                                                         1193 TTCTTATCGGTCTCTGCTTCACTCTTGTCCTGCTCGCCGTCTTCAAACGAGCACTCCCGG
                                                                                                   GCAAGGCTT-----CATCGTACTTTGACTGGAACACGACTATCGCTTGTTATGTGGCCCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          This cDNA clone, deposited as ATCC 97508, codes for human presentlin-1 (hPSI, see AAW23965). Mutations in the presentlin genes have been linked to the development in humans of forms of familial Alzheimer's disease (FAD) and may be causative of other disorders, e.g. cognitive, intellectual, neurological or physiological disorders such as cerebral haemorrhage, schizophrenia, depression,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 presentlin-1 genes - useful for developing
detection, diagnosis and therapy of Alzheimer's
                                                                                                                                                                                                                                                                                                                          Presenilin-1; PS1 gene; human; familial Alzheimer's disease; FAD; cerebral haemorrhage; schizophrenia; depression; epilepsy; mental retardation; diagnosis; therapy; transgenic animal; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               St George-Hyslop PH;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Disclosure; Page 182-185; 238pp; English.
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96US-0021673.
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               ANOVAGES results from alternative splicing of the mRNA transcript in which exon I is directly spliced to exon 3. A mouse PSI in which exon I is directly spliced to exon 3. A mouse PSI in which exon I is directly spliced to exon 3. A mouse PSI in which exon I is directly spliced to exon 3. A mouse PSI exonologue (see AAVO4668) and a human presentlin. 2 sequence (see AAVO4669) are also provided, as well as genomic sequences for the PSI gene (see AAT99661-71). Use of the nucleic acids and proteins comprising or derived from the presentlins is made in screening and diagnosing FAD, identifying and developing therapeutics for treatment of FAD, and in producing cell lines and transgenic animals useful as models of FAD. Nucleic acids (see AAVO4674-80) encoding presentlin interacting proteins are also provided.
                                                                                                                                                                                                                                                                                                                                                                             Score 246.6; DB 19; Length 3086;
Pred. No. 9.1e-47;
0; Mismatches 514; Indels 40;
exon 2 is the
                                                                                                                                                                                                                                                                                                                           Sequence 3086 BP; 789 A; 688 C; 740 G; 866 T; 3 other;
  retardation and epilepsy.
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(PS-I) gene product (see AAW42375). A novel variant of PS-I encoded by a clone isolated from a human cerebellar cDNA library contains a 4-amino acid insertion (VRSQ) between residues 5 and 27. This carbon alternative use of a 5' exon donor site in the exon 3/intron 3 boundary of the PS-I gene. The 4-amino acid motif can be used as a diagnostic marker for variants of presentiln genes associated with Alzheimer's disease and familial adult onset Alzheimer's disease (FAD). Methods are provided for detecting the presence or absence of a 4-amino acid motif (VRXQ, where x is a hydrophilic amino acid) in expressed proteins that arise from aberrant alternative splicing of pre-mRNA in genes associated with normal neurological function, which are useful for detecting neurodegenerative disease. The presence of these variants suggest that mutational events have occurred. Methods to measure the levels of gene expression of such genes to detect neurodegenerative
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                                                                                                                                                                                                                               diseases are provided. Nucleotide sequences and intron-exon junctional sequences of examples of this splicing variant and probes (see AAV03247-49) for detecting this variant which are useful
                                                                                                                                                                                                                                                                                                                                            Length 1750;
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                                                                                                                                                                                                                                                                                                          Sequence 1750 BP; 442 A; 391 C; 428 G; 478 T; 11 other;
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Pred. No. 1.8e-46;
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                                                                                     AACGGGAGCTAGCTGCTGAGAGCCAACTGTACAAGACGCCAATTTTCACAGGCACGAAG 1078
                                                                                                                                                 1079 AGGAAGAGAGAGGTGTGAAACTTGGTCTGGGCGACTTCATTTTCTACTCTGTTCTCCTCG 1138
AAAGCACAGAAAGGGAGTC--ACAAGACACTGTTGCAGAGAATGATGATGGCGGGTTCAG 1554
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"The wild-type PS1 has g replacing the
mutant a at this position"
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The present sequence represents the human mutant S182 gene, PS1 locus.
Mutant PS1 produces a gene product that increases the probability of
Alzheimer's disease. A nucleic acid sequence able to hybridise to
sequences coding for a mutant PS1 polypeptide can be used as probes for
diagnosing an increased likelihood of contracting Alzheimer's disease.
Antibodies against the mutant polypeptide can also be used for this
profesin or antibody specific for mutant PS1 can be administered to a
patient to raduce the likelihood, or delay the onset, of Alzheimer's
cisease, e.g. anti-sense RNA expression can be used to decrease
expression of the PS1 peptide. Transgenic animals expressing the
expression of the PS1 peptide. Transgenic animals expressing the
Alzheimer's disease protein can be used to test candidate therapeutics
and to investigate the normal role of PS1. The PS1 peptide may also be
considered in pharmaceutical compositions (vaccines) for Alzheimer's
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               119 AAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATC 178
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Pred. No. 2e-46;
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Matches 664;
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                                                                                                                                                                     AAAGCACAGAAAGGGAGTC--ACAAGACACTGTTGCAGAGAATGATGATGATGGCGGGTTCAG
                                                                                                                                                                                     959 AAGTGCAAATCGAATCGAATACTACAGCTTCAACGACACAAAACTCTGGAGTAAGGGTGG
                                                                                                                                                                                                                                                  1079 AGGAAGAGAGGTGTGAAACTTGGTCTGGGCGACTTCATTTTCTACTCTGTTCTCCTCG
                                                                                                                                                                                                                                                                                                                          mutation; gene mutant animal; Alzheimer's disease;
                                                                                                                                                                                                                                                                                                                                                                             CCCCATTTGTTACACAAGT 1330
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The present invention describes a gene mutant animal having a non-human mutant presentlin gene. The mutant presentlin gene causes amino acid mutant presentlin gene acuses amino acid substitutions at 1 or more positions 07 79, 82, 96, 115, 120, 135, 139, 146, 163, 209, 213, 231, 235, 246, 250, 260, 263, 264, 267, 269, 280, 285, 286, 290, 318, 384, 392, 410, 426 and 436, with corresponding reminals being e.g. A79V, V82L, A426 and 4365, with corresponding replacing isoleucine of position 13 by another amino-acid especially replacing isoleucine of position 213 by another amino-acid especially threonine. The gene mutant animals e.g. mice can be used as model threonine. The gene mutant animals e.g. mice can be used as model canimals for the study of human Alzheimer's diseases and to screen and evaluate substances as candidates for prevention and/or therapy of Alzheimer's diseases in patients. They can over-produce amyloid the hippocampus earlier. Such animals are being off in the hippocampus earlier. Such animals are being processed to human patients with Alzheimer's diseases. The
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     116 AAGAAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTC 175
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    AACAAGATGAGGAGGAAGAGGATGACATTGAAATATGGAGCCAAGCATGTCATCA 250
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         311 GCTTCTATACCCGGAAGGACG---GTCAGCTAATCTACACCCCATTCACAGAAGACACTG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         AGACTGTAGGCCAAAGAGCCCTGCACTCGATCCTGAATGCGGCCATCATGATCAGTGTCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        416 ATGGATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGC
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                                                                                                                                                                                                                                     ed animals, useful as model animals in human and screening substances
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  present sequence encodes mouse presentlin-1, as given in the present
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Score 243.2; DB 20; Length 1404;
Pred. No. 4.4e-46;
0; Mismatches 498; Indels 42;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Sequence 1404 BP; 354 A; 362 C; 343 G; 345 T; 0 other;
                                                                                                                                                                                                                                                                                       for prevention and/or treatment of the diseases
                                                                                                                                                                                                                                     Mutant presenilin-1 gene-introduced animals,
                                                                                                                                                                                                                                                                                                                                          Disclosure; Page 56-58; 64pp; Japanese.
                                                                                                                                                                                                                                                                 of Alzheimer's diseases
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                                                 (DAUC ) DAIICHI PHARM CO LTD.
98JP-0002191
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Best Local Similarity 54.4
Matches 644; Conservative
                                                                                                       Takeda M;
                                                                                                                                                   WPI; 1999-430307/36.
                                                                                                                                                                                    P-PSDB; AAY24420
08-JAN-1998;
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                                                                                                                                                                                                                                                                   for study
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31-JUL-1995;
28-APR-1995;
28-JUN-1995;
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                                                                                                                                                                                                                                                                                                  CAAAAAGTGCAAATCGAATCGAATACTACAGCTTCAACGACACAAAACTCTGGAGTAAGG 1014
                                                                                                                                                                                                                                                                                                                         GCCATTCTTATCGGTCTCTGCTTCACTCTTGTCCTGCTCGCCGTCTTCAAACGAGCACTC 1248
                                                                                                                                                              GAGAGACACAGGACAGTGGTTCTGGGAACGATGATGGTGGCTTCAGTGAGGAGTGGGAGG 1024
                 904
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Presentlin-1; mouse; hPS1-1; hPS1-2; PS-2; integral membrane protein; AD; familial Alzheimer's disease; cerebral haemorrhage; schizophrenia; depression; antibody; gene expression modulator; therapy; ss.
      AATGGACTGTGTGTTTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCA
                                                                                   AAAACACGACCCCCCGTGAACCGACGTCGTCAGACTCAAATACTTCTACAGCTTTTC
                                                      1015 GTGGAACGGGAGCTAGCTGCTGAGACCAACTGTACAAGACGCCAATTTTCACAGGCAC
                                                                                                                                                                                                                                                               CACCAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAGAAACGAGCCAATTT
                                                                         TCCCGCCCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTG
                                                                                                                                              CTGGAGAGGCGAGTTGTTCATCT-GAAACGCCAAAACGGCCAAAAGTGAAACGAATTCCT
                                                                                                                                                                                                                                                     GAAGAGGAAGAGAGGTGTGAAACTTGGTCTGGGCGACTTCATTTTCTACTCTGTTCTC
                                                                                                                                                                                                CCCAAAGAGACAGTCACCTGGGGCCTCCATCGCTCCA-------
                                                                                                                                                                                                                                                                                       CTCGGCAAGGCTTCATCGTACT-----TTGACTGGAACACGACTATCGCTTGTTATGTG
                                                                                                                                                                                                                                                                                                                                                                   1297 CCAGCCTCCCCATCTCCATCAGCTTCGGGCTCGTGTTCTACTT 1340
                                                                                                                                                                                                                                                                                                                                                           CCGGCTCT-GCAATTICCATTITCTCCGGACTCATTITITACTT 1291
                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Murine presentlin-1 wild type coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Location/Qualifiers
188..1591
/*tag= a
/product= presenilin-1
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                                                                                                                                                                                                                                                                                                                                                                                                                      AAT40030 standard;
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                                                                                                                                                                                                                                                                                                                                                                                                    RESULT 27
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This sequence represents the coding sequence for the murine presentlin-1. AAT40028 and AAT40029 represent the coding sequences for the two different forms of wild type human presentlin-1 (FS-1). The form represented by AAT40029 results from alternate splicing of the genomic DNA sequence. AAT40031 represents the coding sequence for wild type human PS-2. The presentlins are a family of highly conserved integral membrane proteins with a common structural motif, common alternate splicing patterns, and common mutational hot spot regions. Mutations in PS genes are implicated in familial Alzheimer's disease (AD) and possibly other diseases such as cerebral haemorrhage, schizophrenia, depression etc., so detection of mutations in these sequences can be used for diagnosis of these diseases. The encoded proteins, or vectors that express them or containing antisense sequences, antibodies selective for mutant forms of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  116 AAGAAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTC 175
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         176 ATCTATTTGTGCCGGTGTCACTATGCATGGCTCTGGTTGTTTTTACGATGAACACGATTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              438 TGCTCTTTGTCCCCGTGACCCTCTGCATGGTCGTCGTCGTGGCCACCATCAAATCAGTCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      236 CGTTTTATAGTCAAAACAATGGAAGGCATTTACTATCACATCCTTTTGTCCGGGAAACAG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  735 GGGAAGTATTTAAGACCTACAATGTCGCCGTGGACTACGTTACAGTAGCACTCCTAATCT
                                                                                                                                                                                                                                                                                                                                                                              New presenilin genes - useful for diagnosis, therapy and drug screening of familial Alzheimer's disease, cerebral disorders, etc.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       the encoded proteins (such as AAW05736) and modulators of PS gene expression are potentially useful for treatment of AD etc. Transge animals are useful as models for drug screening. The antibodies ca
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           DB 17; Length 1964;
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                                                                                                                                                                                                                          St George-Hyslop PH;
                                                                                                                                                           (UTOR ) UNIV TORONTO GOVERNING COUNCIL.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Claim 8; Page 145-146; 178pp; English.
95US-0509359.
95US-0431048.
95US-0496841.
                                                                                                                                                                                                                          Rommens JM,
                                                                                                                                RES & DEV
                                                                                                                                                                                                                                                                                  WPI; 1996-497631/49.
P-PSDB; AAW05735.
                                                                                                                             (HSCR-) HSC
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us-09-043-944-5.rng

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                                                   AATGGACTGTGTTTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCA
                                                                               CACCAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAAAACGAGCCAATTT
                                                                                                                        776 TCCCGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTG
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                                                                                                                                                                                                                                                                                                                                    GAAGAGGAAGAGAGGTGTGAAACTTGGTĊTGGGCGACTTCATTTTCTACTCTGTTCTC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Presenilin-1; PSI gene; mouse; familial Alzheimer's disease; cerebral haemorrhage; schizophrenia; depression; epilepsy; mental retardation; diagnosis; therapy; transgenic animal; ss
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                                                                                                                                                                                                                                                                                                                      This cDNA clone for a murine presentlin-1 (FS1) homologue (see AAW23966). It was isolated from a mouse cDNA library using a DNA probe from the human PS1 gene (see AAV04666). Mutations in the human PS1 and PS2 genes (see AAV04666-68) have been linked to the development in humans of forms of familial Alzheimer's disease (FAD). All amino acids that are mutated in analysed FAD pedigrees were conserved in the murine homologue. Use of the nucleic acids and proteins comprising or derived from presentlins can be made in screening and diagnosing FAD, identifying and developing therapeutics for treatment of FAD, and in producing cell lines and transgenic animals useful as models of FAD.
                                                                                                                                                                                                                                New isolated mutant presentlin-1 genes - useful for developing products for use in detection, diagnosis and therapy of Alzhelmer's disease and for drug screening
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16.2%; Score 243.2; DB 19; Length 1964;
Best Local Similarity 54.4%; Pred. No. 4.8e-46;
Matches 644; Conservative 0; Mismatches 498; Indels 42;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Sequence 1964 BP; 503 A; 503 C; 496 G; 460 T; 2 other;
                                                                                                                                                       St George-Hyslop PH;
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                                                                                                        (HSCR-) HSC RES & DEV LP.
(UTOR ) UNIV TORONTO GOVERNING COUNCIL.
                                           96US-0021673.
96US-0021700.
96US-0029895.
 97WO-CA00475
                              97US-0034590
                                                                                                                                                        Rommens JM,
                                                                                                                                                                                  WPI; 1998-286355/25.
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                                           05-JUL-1996;
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08-NOV-1996;
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AGGCGTATCTCATTATGATCAGTGCCCTCATGGCCCTGGTATTTATCAAGTACCTCCCCG 914
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                       AATGGACTGTGTGTTTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCA
                                     CACCAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAGAAACGAGCCAATTT
                                                                                    TCCCGGCGCTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTG
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20-DEC-1995;
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                                                                                                                                                                                  This is the nucleotide sequence of the tumour suppressor inhibited pathway gene 2 (TSSIP2). The sequences AAT64813-T64823 represent genes of the tumour suppressor activated pathway (TSAP 1-8, also human TSAP 3, also designated HUMSIAN. i.e. Human Homologue of the Drosophila seven in absentia gene) or of the tumour suppressor inhibited pathway (TSIP 1 and 2). Expression of TSAP genes is induced during apoptosis while that of TSIP is induced by tumour suppressors and inhibited during apoptosis, especially where apoptosis is induced by p53. The sequences, vectors containing them or compounds that induce their expression are useful for are useful as probes and amplification primers to determine predisposition to these diseases by detecting abnormalities in the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     296 ACAGTATCGTTGAGAAGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGG 355
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               116 AAGAAGACGAAAATGTTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTC
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                                                                                                                                                                                                                                                                                                                                                                                                                                        DB 18; Length 2681;
                                                                                         New genes activated or inhibited during apoptosis - useful treatment of, and for assessing risk of developing, cancer Alzheimer's disease
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                                                                                                                                                                                                                                                                                                                                                                                                   Sequence 2681 BP; 663 A; 709 C; 658 G; 650 T; 1 other;
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Pred. No. 5.3e-46;
0; Mismatches 498;
(DAUS-) FOND DAUSSET-CEPH JEAN
                                                                                                                                                   Claim 1; Fig 8; 51pp; French.
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Local Similarity 54.4%;
les 644; Conservative (
                                                          WPI; 1997-341686/31
                           Cohen D,
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                                                                                                                                                                                                                                                                     TCCCGGCGCGTGATTTATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTG
                                                      102 ITCCAGCTCTTATCTATTCCTCAACAATGGTGT---GGTTGGTGAATATGGCTGAAGGAG
                                                                             AAAACACGACACCCCCGTGAACCGACGTCGTCAGACTCAAATACTTCTACAGCTTTTC
                                                                                                   ACCCAGAAGCCCAAAGGAGGGTACCCAAGAACCCCAAGTATAACACACAAAAGAGCGGAGA
                                                                                                                                     219 GAGAGACACAGGACAGTGGTTCTGGGAAGGATGGTGGGAGG
                                                                                                                                                                   CAAAAAGTGCAAATCGAATCGAATACTACAGCTTCAACGACACAAAACTCTGGAGTAAGG
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/*tag= a
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95US-0431048.
95US-0496841.
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28-APR-1995;
28-JUN-1995;
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This sequence represents a homologue of human presentlin, isolated from Drosophila melanogaster. AAT40028 and AAT40029 represent the coding Sequences for the two different forms of wild type human presentinin.

(RS-1). The form represented by AAT40029 results from alternate splicing of the genomic DNA sequence. AAT40031 represents the coding sequence for wild type human PS-2. The presentlins are a family of highly conserved integral membrane proteins with a common structural motif, common alternate splicing patterns, and common mutational hot spot regions.

Mutations in PS genes are implicated in familial Alzheimer's disease (AD) and possibly other diseases such as cerebral haemorrhage, schizophrenia, depression etc., so detection of mutations in these sequences can be used for diagnosis of these diseases. The encoded proteins, or vectors that compares them or containing antisense sequences; antibodies selective for mutant forms of the encoded proteins (such as AAW05736) and modulators of PS gene expression are potentially useful for treatment of AD etc.

Transgenic animals are useful as models for drug screening. The
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                                                                                           New presentlin genes – useful for diagnosis, therapy and drug screening of familial Alzheimer's disease, cerebral disorders,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      DB 17; Length 1895;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 1895 BP; 456 A; 500 C; 468 G; 471 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Score 226.2; DB 17;
Pred. No. 3.8e-42;
0; Mismatches 273;
                PH;
               George-Hyslop
                                                                                                                                          Claim 33; Page 152-154; 178pp; English
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Similarity 59.4%;
33; Conservative (
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                                                                                                                                                                                                                                  Alzheimer's disease; Parkinson's disease; multiple sclerosis; stroke; Huntington's disease; amylotrophic lateral sclerosis; stroke; head injury disease; frontal lobe dementia; cerebellar degeneration; ischaemic injury; schizophrenia; mutant; ss.
                                                                                                                                                                     704 GCACGGATGTCTATCTCCTCTACACACTTTCCATGAACAATCGCCCGAGCCTAGTGTTA
                                                                                                                                    AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG
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/note= "There is an apparent deletion of 4 bases
which alters the reading frame"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          /transl_except= (pos:1152..1154, aa:Xaa)
/transl_except= (pos:1155..1157, aa:Xaa)
/note= "Xaa corresponds to unknown amino acid"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          /*tag= a
/product= "Human mutant presenilin-1 protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              presentlin 1; PS1; amyloid precursor
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   The invention relates to an isolated nucleic acid detection reagent capable of detecting 1000 or more genes from Drosophila. The invention is useful in developmental biology and in elucidating cell signalling and cell-cell interactions in higher enkaryotes for the development of insecticides, therapeutics and pharmaceutical drugs. The invention sequences genomic DNA sequences (ABL16176-ABL30511), expressed DNA (ABB57737-ABB72072).
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    New isolated nucleic acid detection reagent for detecting 1000 or more genes from Drosophila and for elucidating cell signalling and cell-cell
                                                                         TGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCCCGGCGCGTGATTT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             developmental biology; cell signalling; insecticide;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Drosophila melanogaster genomic polynucleotide SEQ ID NO 39184
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al Similarity 59.4%;
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11-JUL-2000; 2000US-0614150.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      The invention relates to mutant presentlin 1 (FS1) and presentlin 2 (FS2) polypeptides. Presentlin are involved in the processing of amyloid precursor protein (APP) from which major amyloidogenic peptides are cleaved. Mutant presentlins are useful for identifying agents that cleaved. Mutant presentlins are useful for identifying agents that modulate amyloid beta-peptide (Abeta) derived peptide production. Mutant presentlin is also useful as a target for screening drugs useful in the prosentlin is also useful as a target for screening drugs useful in the treatment of pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's disease, Parkinson's disease, head injury disease, picks disease, frontal lobe dementia, cerebellar degeneration, stroke, ischaemic injury and schizophrenia. A transgenic non-human animal is useful for analysing the interaction between APP and mutant presentin-processing protease in vivo, and for screening antianimal is useful for analysing the interaction between APP and mutant presentin-processing protease in vivo, and for screening antianianian prelamer's disease drugs in vivo, and for screening antianiant prelamer's disease drugs in vivo, and for screening antianiant prelamer's disease drugs in vivo, The present sequence is human mitant psi constants.
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                                                                                                                                                                                            Novel isolated mutant presenting 1 and presenting 2 polypeptides, useful for screening of drugs for treating pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Sequence 1404 BP; 360 A; 312 C; 336 G; 390 T; 6 other;
                                                                                                                                                                                           Novel isolated mutant presenilin 1 and useful for screening of drugs for treat
                                                                                                                                                                                                                                                              Claim 52; Page 66; 80pp; English.
                                                                                           (PHAA ) PHARMACIA & UPJOHN CO
                                        29-JUN-2001; 2001WO-US16508
                                                                80-JUN-2000; 2000US-215345P
                                                                                                                          Tomasselli AG;
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ACTATGGAGTTCTCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGT
                                                                         GGACTGTGTGTTTTGTGTTTTTTTTTTTCTCGGTTTGGGATCTGGTTGCCGTGCTCACAC
                                                                                                                                                                         CAAAAGGACCATTGAGATATTTGGTGGAAACTGCACAGGAGAGAAACGAGCCAATTTTCC
                                                                                                                                                                                                                                                                                                                              ACACGACAGACCCCGTGAACCGACGTCGACACTCAAATACTTCTACAGCTTTTCCTG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            949 AAAGCACAGAAAGGGAGTC--ACAAGACACTGTTGCAGAGAATGATGATGGCGGGTTCAG
                                                                                                                                                                                                                                                                                                        CGGCGCTGATITATTCGTCTGGAGTCATCTATCCCTACGTTCTTGTTACTGCAGTTGAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             1079 AGGAAGAGAGGTGTGAAACTTGGTCTGGGCGACTTCATTTTCTACTCTGTTCTCCTCG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       TTCTTATCGGTCTCTGCTTCACTCTTGTCCTGCTCGCCGTCTTCAAACGAGCACTCCCGG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    STM2;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    neurodegeneration; senile dementia; human chromosome 1;
Volga German kindred; VG; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Autosomal dominant early-onset Alzheimer's Disease;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Human AD4 protein coding sequence.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              1312 CCCCATTTGTTACACAGT 1330
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               1357 AGCCTTTTATGGACCAATT 1375
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              standard; cDNA; 2236
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948 cciacaargigeccaregacracccaccririereacrercresaacrreges
                                                                                                                                                                        TCAGCAGTTTTCTTCTTTTCCTATTCACTACAATCTATGTGCAAGAAGTTCTGAAAA
                                                                                                   491 GTTTCGATGTGTCTCCCAGCGCACTATTGGTTTTGTTTGGACTGGGTAACTATGGAGTTC
                                                                                                                                                        551 TCGGAATGATGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACCTTATTA
                                                                                                                                                                                                                                                                    671 TIGIGCIGITIGITATCICGGITIGGGAICIGGIIGCCGIGCICACACCAAAAGGACCAI
                                                                731 TGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCCCGGCGCTGATTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Identifying genes which cause chromosome missegregation - useful for identifying causes of and treatments for diseases, e.g. Alzheimer's disease, cancer and ageing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Identifying genes which cause improper chromosome segregation, screening for inhibitors of chromosome missegregation and processes caused by genes encoding chromosome missegregation promoters was exemplified using Alzheimer's disease. The sequences given in AAT87401 to AAT87426 can be used in the above methods.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         AD3; AD4/AD3LP; Alzheimer's disease; chromosome; missegregation; presenilin; inhibitor; AD; trisomy 21; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 BP
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Full AD4/AD3LP sequence.
                                                                                                                                                                                                                                                                                                                                                                                                           1248 ACTCATCTG 1256
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                                                                                                                                                                                                                                                                                                                                                                                 791 ATTCGTCTG 799
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P-PSDB; AAW28508.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Li J, Potter H;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           W09707213-A2.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Homo sapiens.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   15-AUG-1996;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              16-AUG-1995;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                   A genetically isolated group of families with autosomal dominant carly-onset Alzheimer's Disease (AD) has been studied and initial mapping analyses have predicted the AD locus resides on chromosome 1.

The present cDNA sequence corresponds to the wild-type locus (i.e. the AD4 gene, also known as STM2) and was isolated from a human chromosome 1 YAC library. The group of families has been designated from VG individuals and unaffected individuals (from VG and unrelated lineages). Sequence analysis has shown that affected individuals have a nucleotide change at codon 141 resulting in an amino acid alteration from Asn at postition 141 has been replaced by especially one in which Asn at postition. Detection of mutant AD4, cample using antibodies specific for the protein or using nucleic acid probes specific for the mutant gene, provides a means of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           131 ITGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG 190
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            311 AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG 370
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  GCCTCCTCAACTCCGTGCTGAACACCCTCATCATGATCAGCGTCATCGTTATGACCA 827
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                191 TGTCACTATGCATGGCTCTGGTTGTTTTTACGATGAACACGATTACGTTTTATAGTCAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Gaps
                                                                                                                                                                                                                                                                                                                                                                       New Alzheimer's disease related gene, AD4 - used to develop prods. for detecting pre-disposition to or for diagnosis, prevention or treatment of Alzheimer's disease
                                                                                                                                                                                                                                                                                         Levy-Lahad E, Mulligan J, Schellenberg GD;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       15.1%; Score 225.8; DB 18; Length 2236; 59.6%; Pred. No. 4.9e-42;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        3;
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0; Mismatches 267; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Sequence 2236 BP; 488 A; 584 C; 645 G; 519 T; 0 other;
                                         /*tag= a
/product= AD4_protein
              Location/Qualifiers
368..1714
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   diagnosing Alzheimer's disease.
                                                                                                                                                                                                                                 MOLECULAR CORP.
                                                                                                                                                                                                                                                                                                                                                                                                                             Claim 2; Fig 1; 83pp; English.
                                                                                                                                                              95US-0002328.
95US-0000956.
95US-0001675.
                                                                                                                                     96WO-US11386
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                                                                                                                                                                                                                                               GEN HOSPITAL CORP.
VA MEDICAL CENT.
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Matches 399; Conservative
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Wasco W;
                                                                                                                                                                                                                                                                                                                             WPI; 1997-119048/11
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                                                                                                                                    05-JUL-1996;
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28-JUL-1995;
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Tanzi RE,
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                                                                                                                                                                                                                                                                                                                                                                                                                                 TTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAAAAGAACACCAT 730
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Human; presentlin 1; PS1; amyloid precursor protein; APP; drug screening;
Alzheimer's disease; Parkinson's disease; multiple sclerosis; stroke;
Huntington's disease; amylotrophic lateral sclerosis; Picks disease;
head injury disease; frontal lobe dementla; cerebellar degeneration;
                                                                                          131 TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG
                                                                                                        TGTCACTATGCATGGCTCTGGTTGTTTTTACGATGAACACGATTACGTTTTATAGTCAAA
                                                                                                                                                694 TCACTCTGTGCATGATCGTGGTAGCCACCATCAAGTCTGTGCGCTTCTACACAGAGA
                                                                                                                                                                     AGAATGGA----CAGCTCATCTACACGCCATTCACTGAGGACACACCCTCGGTGGGCCAGC
                                                                                                                                                                                                       311 AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG
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            28
 if from the figure legend, the figure and the the specification which sequence of Fig 1 and Fig
                                                         DB 18; Length 2276;
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                                                      15.1%; Score 225.8; DB 18; Length 59.6%; Pred. No. 4.9e-42; .ive 0; Mismatches 267; Indels
                                   Sequence 2276 BP; 494 A; 595 C; 662 G; 525 T; 0 other;
It is not clear from the figure legend,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Human mutant presenilin 1 (PS1) cDNA #3.
                 is the AD4/AD3LP or the AD3 sequence.
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                                                               Best Local Similarity 59.6
Matches 399; Conservative
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          sclosure of
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                                                      Query Match
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The invention relates to mutant presentlin 1 (PS1) and presentlin 2 (PS2) polypeptides. Presentlin are involved in the processing of amyloid precursor protein (APP) from which major amyloidogenic peptides are cleaved. Mutant presentlins are useful for identifying agents that cleaved. Mutant presentlins are useful for identifying agents that modulate amyloid beta-peptide (Abeta) derived peptide production. Mutant presentlin is also useful as a target for screening drugs useful in the treatment of pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, Huntington's disease, amylotrophic lateral sclerosis, head injury disease, picks disease, frontal lobe dementia, cerebellar degeneration, stroke, ischaemic injury and schizophrenia. A transgenic non-human animal is useful for analysing the interaction between APP and mutant presentlin-processing protease in vivo, and for screening antimalism useful for analysing the interaction between APP and mutant presentlin-processing protease in vivo, and for screening antimation mitant presents and processing protease in vivo, and for screening antimation mitant present sequence is human mitant mitant present present sequence is human mitant mitant present sequence is human mitant 
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              178
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Pred. No. 8.1e-42;
0; Mismatches 521;
              SS
ischaemic injury; schizophrenia; mutant;
                                                                                                                                                                                                                                                                                                                                                      Location/Qualifiers
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                       TTTATACCCGGAAGGATG --- GGCAGCTAATCTATACCCCATTCACAGAAGATACCGAGA
                                                  GTATCGTTGAGAAGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTCG
                                                                         371 CTGTGGGCCAGAGGCCCTGCACTCAATTCTGAATGCTGCCATCATGATCAGTGTCATTG
                                                                                                     TTCTGATGACAGTTCTGCTGATTGTTTTCTATAAATACAAGTTTTATAAGCTTATTCATG
                                                                                                                  GATGGCTTATTGTCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAG
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NF-kappa B; neuronal degeneration; spinal muscular atrophy; paralysis; peripheral neuropathy; motorneuron disorder; neurodegenerative disorder; Parkinson; disease; Mentere's disease; multiple sclerosis; Bell's palsy; Huntington's chorea; Down's syndrome amyotrophic lateral sclerosis; ALS; nerve deafness; Alzheimer's disease; epilepsy; ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's syndrome, nerve deafness, Meniere's disease and also for treating peripheral neuropathies, motorneuron disorders such as amyotrophic lateral sclerosis (ALS), Bell's palsy and various conditions involving spinal muscular atrophy and paralysis. The present DNA sequence encodes human presentlin (PS2) protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The invention relates to human Par-4 protein, presentiin protein (PSI and PS2) and their corresponding DNA molecules. The invention also relates to a method for identifying inhibitors of neuronal degeneration, comprising corransfecting eukaryotic host cells expressing presentiin (PS), with a Par-4 DNA, and an NF-kappa B dependent reporter construct, exposing the cotransfected cells to a candidate molecule and monitoring the ability of the candidate molecule to induce NF-kappa B activation. Presentlin proteins participates in nuclear factor kappa B (NF-kappa B) signalling and activation. The inhibitors of neuronal degeneration are useful for traating neurodegenerative disorders such as Alzheimer's
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                                                                                                                                                                                                                                             factor kappa
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                                                                                                                                                                                                                                                                                                                                                                                                                                                  /product- "Human presentiin PS2 protein"
/transl_except= (pos:1051..1052, aa:Glu)
                                                                                                                                                                                                                                             nuclear
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                                                                                                                                                                                                                                           neuroprotective;
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BP
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                                                                                                                                                                                                                                           presenilin; PS2;
                                                                                                    DNA; 1346
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04-JAN-2001; 2001US-0754949.
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                                                                                                                                                                                                         presentlin (PS2) DNA
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                                                                                                                                                                                                                                           Human; Par-4;
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                                                                                                                                                                       24-SEP-2001
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Length 1346;

DB 22;

224.2; DB 2; No. 9.8e-42;

Score ?

14.9%; 59.5%;

Best Local Similarity

Query Match

acid"

/product= "Human mutant presenilin-2 protein"
/transl\_except= (pos:1009.1101, aa:xaa)
/transl\_except= (pos:1102.1104, aa:xaa)
/note= "Xaa corresponds to unknown amino acid

89

Tomasselli

DB,

Carter

WPI; 2002-140082/18.

P-PSDB; AAE17049

29-JUN-2001; 2001WO-US16508 30-JUN-2000; 2000US-215345P (PHAA ) PHARMACIA & UPJOHN

WO200202601-A2

10-JAN-2002

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The invention relates to mutant presentlin 1 (PSI) and presentlin 2 (PS2) polypeptides. Presentlin are involved in the processing of amyloid precursor protein (APP) from which major amyloidogenic peptides are cleaved. Mutant presentlins are useful for identifying agents that cleaved. Mutant presentlins are useful for identifying agents that modulate amyloid beta-peptide (Abeta) derived peptide production. Mutant presentlin is also useful as a target for screening drugs useful in the treatment of pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, Huntington's disease, amylotrophic lateral sclerosis, head injury disease, picks disease, frontal lobe dementia, cerebellar degeneration, stroke, ischaemic injury and schizophremia. A transgenic non-human animal is useful for analysing the interaction between APP and mutant presentlin-processing protease in vivo, and for screening antimal animal is useful for analysing the interaction between APP and mutant presentlin-processing protease in vivo, and for screening antimal is useful for analysing the interaction between APP and mutant presentlin-processing protease in vivo, and for screening antimal is useful for analysing the interaction between APP and mutant presentlin-processing protease in vivo, and for screening antimal mitant presentlin-processing protease in vivo, and for screening antimal mitant presentlin-processing protease in vivo, and for screening antimal mitant presentlin-processing protease in vivo, and for screening antimal mitant present present sequence is human mitant presentlin-processing protease in vivo. The present sequence is human mitant mitant presents.
                                                                                                                                                                                                                                                                                         Novel isolated mutant presentlin 1 and presentlin 2 polypeptides, useful for screening of drugs for treating pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's
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                                           191 TGTCACTATGCATGGCTCTGGTTGTTTTACGATGAACACGATTACGTTTTATAGTCAAA
                                                                                                                                                                                             311 AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTCATGACAG
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Claim 118; Page 72-73; 80pp; English

disease

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                                                                   131 TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG
                                                                                  344 AGAATGGA---CAGCTCATCTACACGACATTCACTGAGGACACACCCTCGGTGGGCCAGC
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                         DB 24; Length 1347;
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                                                 Indels
Sequence 1347 BP; 263 A; 390 C; 388 G; 300 T; 6 other;
                       Score 224.2; DB 24;
Pred. No. 9.8e-42;
0; Mismatches 268;
                                              0;
                       14.9%;
                                             Conservative
                      Query Match
Best Local Similarity
Matches 398; Conserv
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APP; drug screening;

Human; presentlin 2; PS2; amyloid precursor protein; APP; drug 'screeni Alzheimer's disease; Parkinson's disease; multiple sclerosis; stroke; Huntington's disease; amylotrophic.lateral sclerosis; Picks disease; head injury disease; frontal lobe dementia; cerebellar degeneration; ischaemic injury; schizophrenia; mutant; ss.

Location/Qualifiers 1.1347 /\*tag= a

Homo sapiens. Synthetic.

Human mutant presentlin 2 (PS2) cDNA #2.

(first entry)

18-APR-2002

AAD27447;

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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     or
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        preventives for central nervous system (CNS) diseases. The method comprises assaying the inhibitory effect of a test substance on the expression of a splicing variety transcribed from presentlin-2 gene. The method is useful for screening remedies or preventives for CNS diseases, particularly Alzheimer's disease and for diagnosis of the disease. The present sequence represents a splice variant of human presentlin-2 gene.
GTTTCGATGTGTCTCCCAGCGCACTATTGGTTTTGTTTGGACTGGGTAACTATGGAGTTC
                                                CCTACAATGTGGCCATGGACTACCCCACCCTCTTGCTGACTGTCTGGAACTTCGGGCCAG
                                                                       551 TCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACCTTATTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                The invention provides a method for screening and identifying remedies
                                                                                                              Central nervous system; CNS; presenilin-2 gene; screening; human; Alzheimer's disease; splice variant; ss.
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DB 21; Length 1983;

Score 224.2;

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Query Match

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                                  TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG
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               Gaps
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Alzheimer's disease; ss.
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               Indels
Pred. No. 1.1e-41;
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              Conservative
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1069 ACTCATCTG 1077
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 Best Local Similarity
Matches 398; Conserv
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Page 40

us-09-043-944-5.rng

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131 TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG 190
      1230 ACTCATCTG 1238
                                                                                                                                                                                                                                     Key
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   The invention provides a method for screening and identifying remedies or preventives for central nervous system (CNS) diseases. The method comprises assaying the inhibitory effect of a test substance on the expression of a splicing variety transcribed from presentlin-2 gene. The method is useful for screening remedies or preventives for CNS diseases, particularly Alzheimer's disease and for diagnosis of the disease. The present sequence represents the human presentlin-2 gene sequence.
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                                                                                              for remedies or preventives for central nervous system particularly Alzheimer's disease
                                                                                                                                                                                                                                                                                  DB 21; Length 2144;
                                                                                                                                                                                                                                                                           Ouery Match 14.9%; Score 224.2; DB 21; Length Best Local Similarity 59.5%; Pred. No. 1.1e-41; Matches 398; Conservative 0; Mismatches 268; Indels
                                                                                                                                                                                                                                                      Sequence 2144 BP; 461 A; 568 C; 618 G; 497 T; 0 other;
                                                                                                                                                        The invention provides a method for
                                                                                                                                Disclosure; Fig 3; 41pp; Japanese.
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 98JP-0139408
                                                Tohyama
                        (TANA ) TANABE SEIYAKU CO.
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                                              Sato N,
                                                                      WPI; 2000-072440/06
 21-MAY-1998;
                                                                                              Screening
                                              Takagi T,
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This sequence represents the coding sequence for the human presentiin-2.
AAV40028 and AAY40029 represent the coding sequences for the two
different forms of wild type human presentiin-1 (PS-1). The form
represented by AAY40029 results from alternate splicing of the genomic
DNA sequence. AAT40030 represents the coding sequence for wild type mouse
PS-1. The presentilins are a family of highly conserved integral membrane
proteins with a common structural motif, common alternate splicing
patterns, and common mutational hot spot regions. Mutations in PS genes
are implicated in familial Alzheimer's disease. (Ab) and possibly other
diseases such as cerebral haemorrhade, schizophrenia, depression etc., so
detection of mutations in these sequences can be used for diagnosis of
these diseases. The encoded proteins, or vectors that express them or
containing antisense sequences, antibodies selective for mutant forms of
the encoded proteins (such as AAW05736) and modulators of PS gene
expression are potentially useful for treatment of AD etc. Transgenic
animals are useful as models for drug screening. The antibodies can also
be used e.g. for affinity purification and in immunoassays.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Ä
                                                                                                                                                                                                                                                                                                                   AD;
                                                                                                                                                                                                                                                                                                       Presenilin-2; human; hPS1-1; hPS1-2; PS-2; integral membrane protein; familial Alzheimer's disease; cerebral haemorrhage; schizophrenia; depression; antibody; gene expression modulator; therapy; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        New presentlin genes - useful for diagnosis, therapy and drug screening of familial Alzheimer's disease, cerebral disorders, etc.
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14.9%; Score 224.2; DB 17; Length 2229;
Best Local Similarity 59.5%; Pred. No. 1.1e-41;
Matches 398; Conservative 0; Mismatches 268; Indels 3;
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                                                                                                                                                                                                                               Human presenilin-2 wild type coding sequence.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              /product- presentlin-2
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366..1712
AAT40031 standard; DNA; 2229
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95US-0496841.
                                                                                                                                                   25-JUL-1997 (first entry)
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589 IGGAGGAAGACCICAACCICAAATACGGAGCGAAGCAIGIGAICAIGCIGITIGIGCCIG 648
                                                                                                  GCCTCCTCAACTCCGTGCTGAACACCCTCATCATGATCAGGGTCATCGTGGTTATGACCA
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              TGTCACTATGCATGCTCTGGTTGTTTTACGATGAACACGATTACGTTTTATAGTCAAA
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366..1715
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This CUMP actions, deposited as ALC 7/21%, codes Lot numeral trains CUMP actions of the AMZ-2967). Mutations in the presentlin genes have been linked to the development in humans of forms of familial Alzheimer's disease (FAD) and may be causative of other disorders, c.g. cognitive, intellectual, neurological or physiological disorders such as cerebral haemorrhage, schizophrenia, depression, mental retardation and epilepsy. hPS2 cDNA has been obtained from Coaco cancer and human PS1 gene. The PS2 gene maps to chromosome 1. Human hPS1 sequences (see AAV04666-67) are also disclosed. Use of the nucleic acids and proteins comprising or derived from the presentlins is made in screening and diagnosing cereby, identifying and developing therapeutics for treatment of FAD, and in producing cell lines and transgenic animals useful as models of FAD. International actions (see AAV04641-80) encoding presentlin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            131 TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG 190
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    DB 19; Length 2229;
                       to C FAD mutation site (Ile420Thr)"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Indels
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Pred. No. 1.1e-41;
0; Mismatches 268;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         St George-Hyslop PH;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Disclosure; Page 201-203; 238pp; English.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Human; beta-amyloid precursor protein; beta-APP; diagnosis; cancer; frameshift mutation; age-related disease; neurodegenerative disorder; Alzheimer, s disease; Down's syndrome; myotonic dystrophy; neuronal; Huntington's disease; multiple sclerosis, alcoholic liver disease; diabetes mellitus type II; microtubule associated protein; Tau; Big Tau; neurofilament-E; presentlin II; cellular tumour antigen; qlial fibrillary acidic protein; GRSP; p53; semaphorin III; HUFF-I; bcl-2; B-cell leukemia/lymphoma 2 proto-oncogene; HMGP-C; NSP-A; high mobility group protein-C; neuroendocrine specific protein A; ss.
                                                                                                                                                         1066 TGATCAGTGCGCTCATGGCCCTAGTGTTCATCAAGTACCTCCCCAGAGTGGTCGCGCGTGGG
                          491 GTTTCGATGTGTCTCCCAGCGCACTATTGGTTTTGTTTGGACTGGGTAACTATGGAGTTC
                                                       946 ccracaardregeccargeacraccccaccrtrrecreacrerregaacrrcegegege
                                                                                   TCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACTTA
                                                                                                                                          731 TGAGATATTTGGTGGAAACTGCACAGGAGAGAAACGAGCCAATTTTCCCGGCGCTGATTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Diagnosing disease by detecting frameshift mutations in RNA or corresponding protein mutations - used to diagnose cancer and neurological diseases, particularly Alzheimer's disease, and also for treatment and prevention with specific ribozymes or wild-type
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(ROYA-) ROYAL NETHERLANDS ACAD ARTS & SCI.
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|246 ACTCATCTG 1254
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This invention describes a novel method for the diagnosis of a disease caused by, or associated with, an RNA molecule that has a frameshift mutation. The method is used to diagnose age-related diseases, equation. The method is used to diagnose age-related diseases, e.g. especially cancer and a wide range of neurodegenerative disorders (e.g. Alzheimer's disease, Down's syndrome, myotonic dystrophy, Huntington's disease, multiple sclerosis, alcoholic liver disease, diabetes mellitus contains and many others listed) or susceptibility to these disorders. The method allows a definitive diagnosis of Alzheimer's disease in living patients, at an early stage. It is based on the observation that disease contains and partial system RNA molecules, specifically proteins including beta amyloid precursor protein (beta-App), the content of microtubule associated protein zone protein (beta-App), the microfilament-L, neurofilament-R, neurofilament-F, presentlin I, glial fibrillary acidic protein (GFAP), the cellular tumour antigen pay Each leukemia/lymphoma 2 (bcl.2) proto-oncogene, semaphorin III, HUPF-I, high mobility group protein-C (HMGP-C) and mutant protein fragments represented in ANY20896-Y20955.
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Pred. No. 1.1e-41;
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791 ATTCGTCTG 799

Disclosure; Figure 11; 258pp; English

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948 ccracaargragacargaacracccaccrargaacrargaaacracagagaa 1007
                                                                                                                                                                                                                                                                                                                 GTTTCGATGTCTCCCAGCGCACTATTGGTTTGTTTGGACTGGGTAACTATGGAGTTC 550
                                                                                            311 AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG 370
                                                                                                           TCAGCAGTTTTCTTCTTTTCCTATTCACTACAATCTATGTGCAAGAAGTTCTGAAAA 490
                                                                    AGAATGGA----CAGCTCATCTACACGACATTCACTGAGGACACACCCTCGGTGGGCCAGC 767
                                           551 TCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACTTATTA
                                                                                                                                                                                                                                                                                                                                                                                                          671 TTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACACCAAAAGGACCAT
                                                                                                                                                                                                                                                                                                                                                       731 TGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCCCGGCGCGTGATTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 SS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           KIAA0253; presenilin; Alzheimer's disease;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    /product= "presenilin 2"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Nucleotide sequence of human presenilin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Location/Qualifiers
368..1714
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      AAH74994 standard; DNA; 2236 BP
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              09-MAR-2001; 2001WO-GB01057
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                1248 ACTCATCTG 1256
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 (GLAX ) GLAXO GROUP LTD.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               791 ATTCGTCTG 799
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    The invention relates to a method for identifying modulators of presentiin and catenin pl20. Modulators of catenin pl20 and presentiin are useful for the treatment and prophylaxis of disorders that is responsive to modulation of presentiln/catenin pl20 activity. In particular, neuronal disorders such as cognitive disorders and neurodegenerative diseases such as Alzheimer's disease. Catenin pl20 bnAs are useful for identifying mutations in catenin pl20 genes. Identification of such mutations assist in the diagnosis of or susceptibility to Alzheimer's or other conditions associated with presentlin and in assessing the physiology of such disorders. Catenin pl20 bnAs are also used in hybridisation studies to monitor expression of pl20 genes and in particular for up or down regulation of catenin pl20 expression. The present DNA sequence encodes human presentlin-2 (PS-2)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  650
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     191 IGTCACTATGCATGGCTCTGGTTGTTTTACGATGAACACGATTACGTTTTATAGTCAAA 250
                                                                                                                                                                              Human; catenin pl20; presenilin-2; PS-2; neuroprotective; gene therapy; neurodegenerative disease; Alzheimer's disease; nootropic; prophylaxis; neuronal disorder; cognitive disorder; ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTTTTGTGCCGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Identifying presentlin or catenin p120 activity modulator useful for modulating presentlin-catenin p120 interaction and thus for treating cognitive disorder e.g., Alzheimer's disease comprises enhancing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Gaps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Score 224.2; DB 22; Length
Pred. No. 1.1e-41;
0; Mismatches 268; Indels
                                                                                                                                                                                                                                                                                                /product= "Human presenilin-2 protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 2236 BP; 490 A; 583 C; 645 G; 518 T; 0 other;
                                                                                                                                                     Human presenilin-2 (PS-2) protein DNA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Disclosure; Page 46-48; 48pp; English.
                                                                                                                                                                                                                                                           Location/Qualifiers
368..1714
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                                                                            BP.
                                                                                                                                                                                                                                                                                                                                                                                                                                                        Blackstock
                                                                           DNA; 2236
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59.5%;
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                                                                                                                             (first entry)
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1248 ACTCATCTG 1256
                                                                                                                                                                                                                                                                                                                                                                                                                              (GLAX ) GLAXO GROUP LTD.
                                                                                                                                                                                                                                                                                     /*tag=
                                                                                                                                                                                                                                                                                                                                                                                                                                                      Hale RS, Rowley A,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                             WPI; 2001-589954/66.
P-PSDB; AAE10799.
                                                                          AAD18121 standard;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          cognitive function
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nes 398; Conserv
                                                                                                                                                                                                                                                                                                                        WO200167097-A2
                                                                                                                           18-DEC-2001
                                                                                                                                                                                                                                  Homo sapiens
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                                                                                                   AAD18121;
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Best Local S
Matches 398
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TIGIGGAAGAAGCGGAGCIGAAAIACGGAGCAICICACGTIAITCAICITIIGIGCCGG 190
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                311 AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG 370
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       TCAGCAGTITICTICTITITCCIATICACTACAATCIATGTGCAAGAAGTICTGAAAA 490
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   888 TGTCTTCACTGATGCTGCTGTTCCTCTTCACTATCTACCTTGGGGAAGTGCTCAAGA 947
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     TIGIGCICITITGITATCICGGITIGGGAICIGGIIGCCGIGCICACACCAAAGGACCAI 730
                                                                                                                                                                                                                  Identifying a modulator of presentiin function by determining the ability of presentlin to bind to a K1AA0253 polypeptide in the presence and absence of a test compound, useful in the treatment or prophylaxis
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           The present sequence encodes human presentlin 2. KIAA0253 binds to presentlin. The specification describes a method of identifying a modulator of presentlin function or KIAA0253 function. The method comprises determining presentlin activity or KIAA0253 activity and the presence and absence of a test compound, where presentlin activity is determined by its ability to bind to KIAA0253. A modulator of presentlin or KIAA0253 polypeptide is useful in the manufacture of a medicament for the treatment or prophylaxis of Alzheimer's disease. The KIAA0253 polynucleotide and KIAA0253 polypeptide are useful in the treatment, prophylaxis of Alzheimer's disease.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       TGTCACTATGCATGGCTCTGGTTGTTTTTACGATGAACACGATTACGTTTATAGTCAAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         TCTTCTTGGTGGTGCTCTACAAGTACCGCTGCTACAAGTTCATCCATGGCTGGTTGATCA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    0; Mismatches 268; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sequence 2236 BP; 490 A; 583 C; 645 G; 518 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Score 224.2; DB 2;
Pred. No. 1.1e-41;
                                                                                                                                                                                                                                                                                                                                                                                                                                    Disclosure; Page 44-47; 48pp; English.
         Blackstock
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              14.9%;
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398; Conservative
                                                                                                                                                                                                                                                                                                         and absence of a test cor
of Alzheimer's disease .
    Rowley A,
                                                                                      2001-522960/57
                                                                                                                                P-PSDB; AAG63937
    Hale RS,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Query Match
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proteins from a variety of organisms, including human, dog, cat, horse, cow, plg, hamster, monkey, macaque, yeast, bacteria, fruit fly, sea urchin and tomator. These were derived from expressed sequence tags (ESTs) from the organism of interest. They can be used in diagnostics, forensics, gene mapping, identification of mutations, to assess biodiversity and for nutritional purposes. The present sequence is a cDNA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             131 ITGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    672 TCACTCTGTGCATGATCGTGGTGGTAGCCACCATCAAGTCTGTGCGCTTCTACACAGAGA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Isolated polypeptide for treatment of diseases, diagnostics, raising antibodies and research use \boldsymbol{\cdot}
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Gaps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                     ;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             DB 22; Length 2527;
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                                                                                                                                                                                                 Human; sheep; pig; cow; fruit fly; yeast; hamster; macaque; tomato; monkey; dog; sea urchin; expressed sequence tag; EST diagnostics; forensic test; gene mapping; genetic disorder; biodiversity; gene therapy; nutrition; ss.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Chen
                                                                                                                                                                        Human EST-derived coding sequence SEQ ID NO: 337
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            14.9%; Score 224.2; DB 2 59.5%; Pred. No. 1.2e-41;
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Werhman T;
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Zhang J, Werh
                                                                                             BP.
                                                                                         AAH98480 standard; cDNA; 2527
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2000US-0631451.
2000US-063870.
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                        ACTCATCTG 1256
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791 ATTCGTCTG
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                                                                                                                                                                                                                                                                                            WO200154477-A2.
                                                                                                                                                                                                                                                                   Homo sapiens.
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15-SEP-2000;
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                                                                                                                     AAH98480;
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AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG
           TCAGCAGTTTTCTTCTTTTCCTATTCACTACAATCTATGTGCAAGAAGTTCTGAAAA
                                                                                                                   TGTCTTCACTGATGCTGCTGTTCCTCTTCACCTATATCTACCTTGGGGAAGTGCTCAAGA
                                                                                                                                                   GTTTCGATGTGTCTCCCAGCGCACTATTGGTTTTGTTTGGACTGGGTAACTATGGAGTTC
                                                                                                                                                                           CCTACAATGTGGCCATGGACTACCCCACCCTCTTGCTGACTGTCTGGAACTTCGGGGCCAG
                                                                                                                                                                                                      TCGGAATGATGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACCTTATTA
                                                                                                                                                                                                                  1029 TGGGCATGGTGTGCATCCACTGGAAGGCCCTCTGGTGCTGCAGCCGAGCCTACCTCATCA
                                                                                                                                                                                                                                                       .089 TGATCAGTGCGCTCATGGCCCTAGTGTTCATCAAGTACCTCCCAGAGTGGTCCGCGTGGG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Alzheimer's disease; Parkinson's disease; multiple sclerosis; stroke;
Huntington's disease; amylotrophic lateral sclerosis; Picks disease;
head injury disease; frontal lobe dementia; cerebellar degeneration;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              /*tag= a
/product= "Human mutant presentlin-2 protein"
/transl_except= (pos:790..792, aa:Xaa)
/transl_except= (pos:793..795, aa:Xaa)
/note= "Xaa corresponds to unknown amino acid"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ischaemic injury; schizophrenia; mutant; ss
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Human mutant presenilin 2 (PS2) cDNA #1.
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1..1347
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(PS2) polypeptides. Presenting a reinvolved in the processing of amyloid precursor protein (APP) from which major amyloidogenic peptides are cleaved. Mutrant presenting are useful for identifying agents that modulate amyloid beta-peptide (Abeta) derived peptide production. Mutant presentin is also useful as a target for screening drugs useful in the treatment of pathologies associated with aberrant amyloid precursor multiple sclerosis, Huntington's disease, parkinson's disease, multiple sclerosis, Huntington's disease, frontal lobe dementia, cerebellar degeneration, stroke, ischaemic injury and schizophrenia. A transgenic non-human animal is useful for analysing the interaction between APP and mutant presentilin-processing protease in vivo, and for screening anti-chimal is useful for analysing the interaction between APP and mutant presentilin-processing protease in vivo, and for screening anti-chimal is useful for analysing the interaction between APP and mutant presentilin-processing protease in vivo, and for screening anti-chimal is useful for analysing the interaction between APP and mutant presentilin-processing protease in vivo, and for screening anti-chimal is useful for analysing the interaction between APP and mutant presentilin-processing protease in vivo, and for screening anti-chimal animal is useful for analysing the interaction between APP and mutant presentilin-processing protease in vivo, and for screening anti-chimal animal 
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                                                                                                                                        Novel isolated mutant presenilin 1 and presenilin 2 polypeptides, useful for screening of drugs for treating pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              131 TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCACGTTATTCATCTATTTGTGCCGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             191 TGTCACTATGCATGGCTCTGGTTGTTTTACGATGAACACGATTACGTTTATAGTCAAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               344 AGAATGGA---CAGCTCATCTACACGACATTCACTGAGGACACACCCTCGGTGGGCCAGC
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                                                                                                                                                                                                                                                                                                                 invention relates to mutant presenilin 1 (PS1) and presenilin 2
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 DB 24; Length 1347;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sequence 1347 BP; 264 A; 390 C; 386 G; 301 T; 6 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Score 221.4; DB 24;
Pred. No. 4.3e-41;
); Mismatches 272;
                                                                                                                                                                                                                                                               72; 80pp; English
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ilarity 58.9%;
Conservative (
                    AG;
                    Tomasselli
                                                                 2002-140082/18.
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Matches 394; Conserv
                                                                                     P-PSDB; AAE17048
                                                                                                                                                                                                                                                            Claim 110; Page
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   mutant PS2 cDNA.
                    DB,
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              Human; presentlin 2; PS2; amyloid precursor protein; APP; drug screening; Alzheimer's disease; Parkinson's disease; multiple sclerosis; stroke; Huntington's disease; amylotrophic lateral sclerosis; Picks disease; head injury disease; frontal lobe dementa; cerebellar degeneration; ischaemic injury; schizophrenia; mutant; ss.
  TTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACACCAAAAGGACCAT 730
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  with
                                     TGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCCCGGCGCTGATTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Novel isolated mutant presentlin 1 and presentlin 2 polypeptides, useful for screening of drugs for treating pathologies associated waberrant amyloid precursor protein processing, such as Alzheimer's
                                                                                                                                                                                                                                                                                                                   /product = "Human mutant presentlin-2 protein"
/transl_except = (pos:790..792, aa:Xaa)
/transl_except = (pos:193..795, aa:Xaa)
/transl_except = (pos:1009..1101, aa:Xaa)
/transl_except = (pos:1102..1104, aa:Xaa)
/note = "Xaa corresponds to unknown amino acid"
                                                                                                                                                                                          Human mutant presentlin 2 (PS2) cDNA #3.
                                                                                                                                                                                                                                                                                          Location/Qualifiers
1..1347
/*tag= a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Claim 126; Page 73; 80pp; English.
                                                                                                                                       BP
                                                                                                                                   AAD27448 standard; cDNA; 1347
                                                                                                                                                                                                                                                                                                                                                                                                                                                       (PHAA ) PHARMACIA & UPJOHN CO.
                                                                                                                                                                                                                                                                                                                                                                                                                                      2000US-215345P.
                                                                                                                                                                                                                                                                                                                                                                                                                    29-JUN-2001; 2001WO-US16508
                                                                                                                                                                        (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Tomasselli AG;
                                                                          ATTCGTCTG 799
                                                                                           ACTCATCTG 889
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         2002-140082/18.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   P-PSDB; AAE17050
                                                                                                                                                                                                                                                                                                                                                                                 WO200202601-A2.
                                                                                                                                                                                                                                                                Homo sapiens
                                                                                                                                                                                                                                                                                                                                                                                                                                     30-JUN-2000;
                                                                                                                                                                       18-APR-2002
                                                                                                                                                                                                                                                                                                                                                                                                   10-JAN-2002.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Carter DB,
                                     731
                                                                                                                                                                                                                                                                          Synthetic
                                                                         791
                                                                                                                                                      AAD27448;
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                                                                                                                   RESULT 47
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The invention relates to mutant presentiin 1 (PSI) and presentiin 2 (PS2) polypeptides. Presentiin are involved in the processing of amyloid precursor protein (APP) from which major amyloidogenic peptides are cleaved. Mutant presentiins are useful for identifying agents that modulate amyloid beta-peptide (Abeta) derived peptide production. Mutant presentlin is also useful as a target for screening drugs useful in the treatment of pathologies associated with aberrant amyloid precursor protein processing, such as Alzheimer's disease, Parkinson's disease,

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190
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  370
multiple sclerosis, Huntington's disease, amylotrophic lateral sclerosis, head injury disease, Picks disease, frontal lobe dementia, cerebellar degeneration, stroke, ischaemic injury and schizophrenia. A transgenic non-human animal is useful for analysing the interaction between APP and Mutant presentiin-processing protease in vivo, and for screening antiallableance,'s disease drugs in vivo. A transgenic non-human animal is useful for analysing the interaction between APP and mutant presentiin-processing protease in vivo, and for screening antipresentilin-processing protease in vivo, and for screening anti-matant presentilin-processing protease in vivo. The present sequence is human
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                490
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       491 GITTCGATGTGTCTCCCAGGGGACTATTGGTTTTGTTTGGACTGGGTAACTATGGAGTTC 550
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      131 TIGIGGAAGAAGCGGAGCIGAAATACGGAGCAICICACGITATICAICIAITIGIGCCGG
                                                                                                                                                                                                                                                                                                                                                                      TGTCACTATGCATGGCTCTGGTTGTTTTACGATGAACACGATTACGTTTTATAGTCAAA
                                                                                                                                                                                                                                                                                                                                                                                                       284 TCACTCTGTGCATGATCGTGGTGGTAGCCACCATCAAGTCTGTGCGCTTCTACACAGAGA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   TCAGCAGTTTTCTTCTTTTCCTATTCACTACTATCTATGTGCAAGAAGTTCTGAAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           581 CCTACAATGTGGCCATGGACTACCCCACCCTCTTGCTGACTGCTGGAACTTCGGGGCAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        551 TCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACCTTATTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   TTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACACCAAAAGGACCAT
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                                                                                                                                                                                                                              Score 221.4; DB 24; Length
Pred. No. 4.3e-41;
0; Mismatches 272; Indels
                                                                                                                                                                                             Sequence 1347 BP; 263 A; 388 C; 386 G; 298 T; 12 other;
                                                                                                                                                                                                                 14.8%; Scor.
58.9%; Pred
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                                                                                                                                                              mutant PS2 cDNA
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                                                                                                                                                                                                                               Query Match
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TTGTGCTGTTTGTTATCTCGGTTTGGGATCTGGTTGCCGTGCTCACAAAAGGACCAT 730
                                                                                                                                                           TGAGATATTTGGTGGAAACTGCACAGGAGAAACGAGCCAATTTTCCCGGCGCTGATTT 790
                                                                                                                                                                       TCGGAATGATGTGTATACATTGGAAAGGTCCATTGCGTCTGCAACAGTTCTACCTTATTA
                                                564 IGAICCIGGCGCCCAICICIGIGIAIGAICICGIGACIGICCIGIGITICCACAGGGCCIC
                                                                                          Central nervous system; CNS; presenilin-2 gene; screening; human;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Screening for remedies or preventives for central nervous system diseases, particularly Alzheimer's disease
                                                                                                                                                                                                                                                                                                                                      presenilin-2 gene splice variant 3.
                                                                                                                                                                                                                                                                                                                                                                    Alzheimer's disease; splice variant; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Claim 18; Page 36-37; 41pp; Japanese.
                                                                                                                                                                                                                                                                            BP.
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                                                                                                                                                                                                                                                                                                                  (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            (TANA ) TANABE SEIYAKU CO
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Matches 296; Conservative
                                                                                                                                                                                                                 ACTCATCT 691
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  WPI; 2000-072440/06
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sato N,
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                                                                                                                                                                                                                                                                                                                                                                                         Homo sapiens
                                                                                                                                                                                                                                                                                                                                                                                                           WO9960122-A1
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      98
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            131 TTGTGGAAGAAGCGGAGCTGAAATACGGAGCATCTCCACGTTATTCATCTATTTGTGCCGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               311 AGGGATTGATGTCACTTGGAAATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    191 TGTCACTATGCATGGCTCTGGTTGTTTTACGATGAACACGATTACGTTTTATAGTCAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          TCAGCAGTTTTCTTCTTTTTCCTATTCACTACAATCTATGTGCAAGAAGTTCTGAAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        rgrcrrcargargcrgcrgrrccrcrrcaccrararcraccrrgggaagrgcrcaaga
                                                                                                                                                                                                                                                                            Identifying genes which cause chromosome missegregation - useful for identifying causes of and treatments for diseases, e.g. Alzheimer's
                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Gaps
                                                                                                                                                                                                                                                                                                                                                screening for inhibitors of chromosome missegregation and processes caused by genes encoding chromosome missegregation promoters was exemplified using Alzheiner's disease. The sequences given in AAY87401 to AAY87426 can be used in the above methods. It is not clear from the figure legend, the figure and the disclosure of the specification which sequence of Fig 1 and Fig 28
                                 chromosome; missegregation;
                                                                                                                                                                                                                                                                                                                                                                                                                                                         DB 18; Length 1417;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                              3;
                                                                                                                                                                                                                                                                                                                                              segredation,
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es 287; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                               Sequence 1417 BP; 307 A; 385 C; 380 G; 345 T; 0 other;
                                                                                                                                                                                                                                                                                                                                       Identifying genes which cause improper chromosome
                                                                                                                                                                                                                                                                                                                                                                                                                                                                Pred. No. 1.6e
0; Mismatches
                            AD3; AD4/AD3LP; Alzheimer's disease; chron
presenilin; inhibitor; AD; trisomy.21; ss
                                                                                                                                                                                                                                                                                                                                                                                                                                                       Score 192.8;
                                                                                                                                                                                                                                                                                                                                                                                                              the AD4/AD3LP or the AD3 sequence
                                                                                Location/Qualifiers
1.1132
/*tag= a
                                                                                                                                                                                                                                                                                                                  Claim 16; Fig 1; 77pp; English.
                                                                                                                                                               96WO-US13314
                                                                                                                                                                                   95US-0002448
                                                                                                                                                                                                                                                                                                                                                                                                                                                    Query Match 12.9%;
Best Local Similarity 56.6%;
Matches 378; Conservative
                                                                                                                                                                                                                                                                                                disease, cancer and ageing
                                                                                                                                                                                                     (HARD ) HARVARD COLLEGE.
                                                                                                                                                                                                                                              WPI; 1997-165297/15.
          AD4/AD3LP sequence
                                                                                                                                                                                                                           Potter H;
                                                                                                                                                                                                                                                          P-PSDB; AAW28506
                                                            sapiens
                                                                                                                     WO9707213-A2
                                                                                                                                                               15-AUG-1996;
                                                                                                                                                                                  16-AUG-1995;
                                                                                                                                         27-FEB-1997
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ö or 331 AATGCTCTCGTCATGTTGTGCGTGGTCGTTCTGATGACAGTTCTGCTGATGTTTTTCTAT 390 The invention provides a method for screening and identifying remedies or preventives for central nervous system (CNS) diseases. The method comprises assaying the inhibitory effect of a test substance on the expression of a splicing variety transcribed from presentlin-2 gene. The method is useful for screening remedies or preventives for CNS diseases, particularly Alzheimer's disease and for diagnosis of the disease. The present sequence represents a splice variant of human presentlin-2 gene. DB 21; Length 1848; Sequence 1848 BP; 393 A; 497 C; 513 G; 445 T; 0 other; 12.8%; Score 192.2; DB 21; 63.1%; Pred. No. 2.4e-34; Live 0; Mismatches 173;

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533
                                                     593
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                                  450
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                                                                                                                                                                                                                                      GTTTGGGATCTGGTTGCCGTGCTCACACAAAGGACCATTGAGATATTTGGTGGAAACT 750
                                                                                                                             TGGAAAGGICCATTGCGTCTGCAACAGTTCTACCTTATTACAATGTCTGCACTAATGGCT 630
                                                                                                                                                                      714 TGGAAGGGCCCTCTGGTGCTGCAGCCTACCTCATCATGATCAGTGCGCTCATGGCC 773
                                                                                                                                                                                                CIGGICITITAICAAGTACCTACCAGAATGGACTGTGTGGTTTTGTGCTGTTTTGTTATCTCG 690
AAATACAAGTTTTATAAGCTTATTCATGGATGGCTTATTGTCAGCAGTTTTCTTCTT
                                                   AAGTACCGCTGCTACAAGTTCATCCATGGCTGGTTGATCATGTCTTCACTGATGCTGCTG
                                                                                         Trecretreaceratareracerregegaagreereaagaeeracaargregeearegae
                                                                                                               511 GCACTATTGGTTTTGTTTGGACTGGGTAACTATGGAGTTCTCGGAATGATGTGTATACAT
                                                                                                                                                                                                           TTCCTATTCACTACAATCTATGTGCAAGAAGTTCTGAAAAGTTTCGATGTGTCTCCCAGC
                                                                                                                                                                                                                                                                                                                                                                                                                                     Central nervous system; CNS; presenilin-2 gene; screening; human;
Alzheimer's disease; splice variant; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Screening for remedies or preventives for central nervous system diseases, particularly Alzheimer's disease
                                                                                                                                                                                                                                                                              GCACAGGAGAAACGAGCCAATTTTCCCGGCGCTGATTTATTCGTCTG 799
                                                                                                                                                                                                                                                                                          Human presenilin-2 gene splice variant 1.
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                                                                                                                                                                                                                                                                                                                                                     AAZ40669 standard; DNA; 2002 BP
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remedies or

preventives for central nervous system (CNS) diseases. The method comprises assaying the inhibitory effect of a test substance on the expression of a splicing variety transcribed from presentlin-2 gene. The method is useful for screening remedies or preventives for CNS diseases, satticularly Alzheimer's disease and for diagnosis of the disease. The present sequence represents a splice variant of human presentlin-2 gene.

invention provides a method for screening and identifying

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